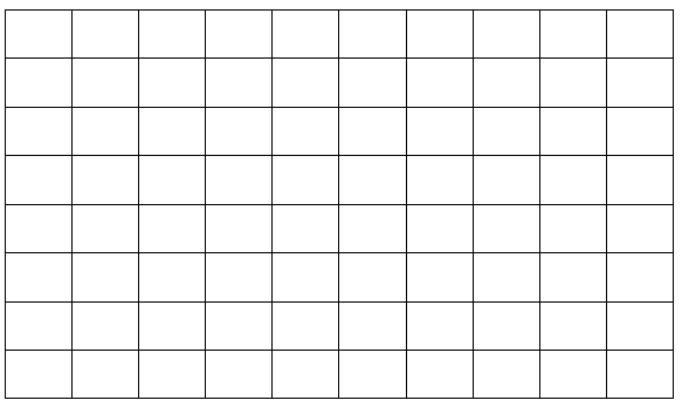
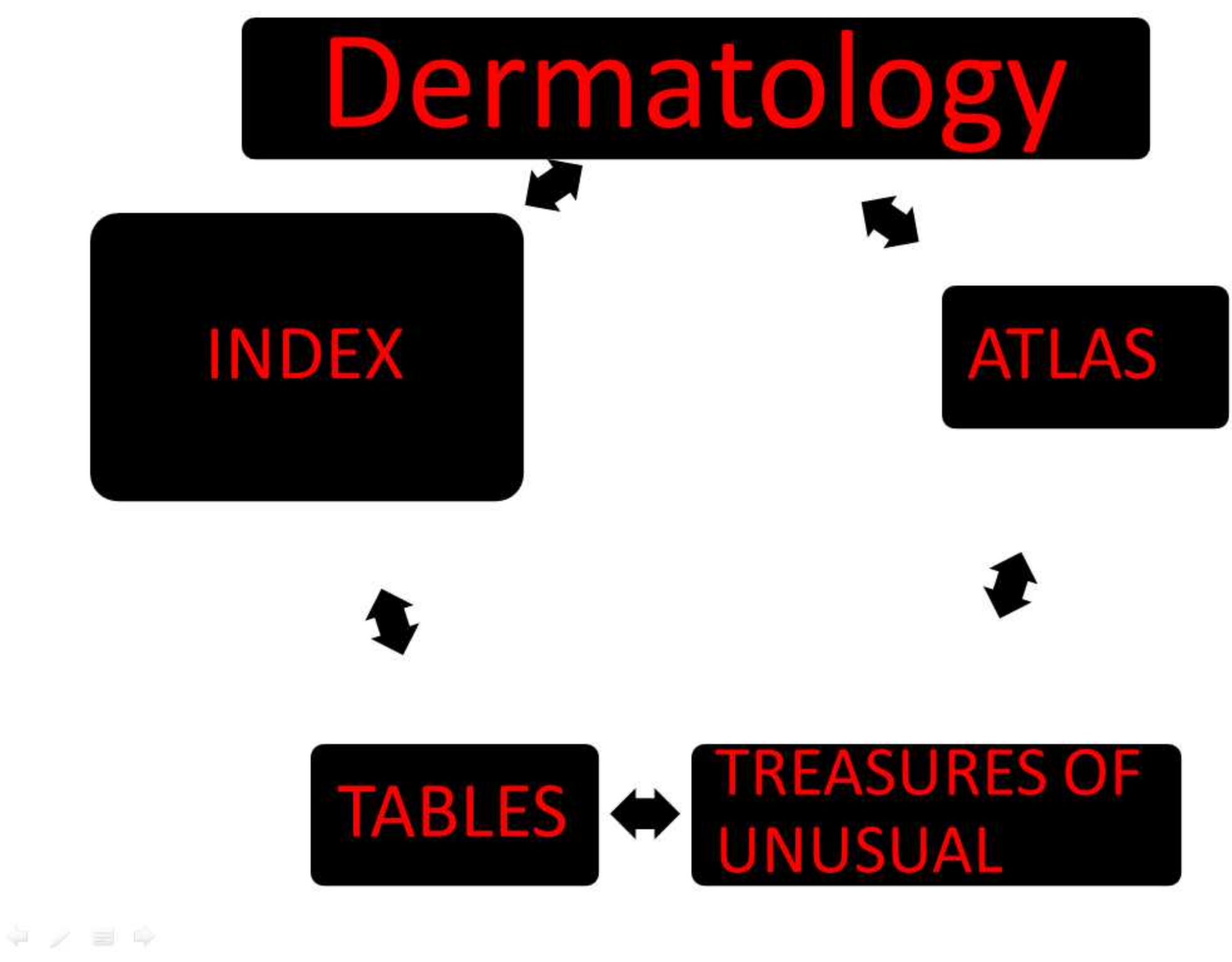
Tables in Dermatology

+15 THOUSANDS TABLES

H.S.S-Mansoura-Egypt`



Whatsapp +201061732403


Dermatology
INDEX
ATLAS
TABLES
TREASURES OF UNUSUAL

بسم الله الرحمن الرحيم

وسلم وصلى على الله

الله جل جلاله

جل جلاله

الله جل جلاله

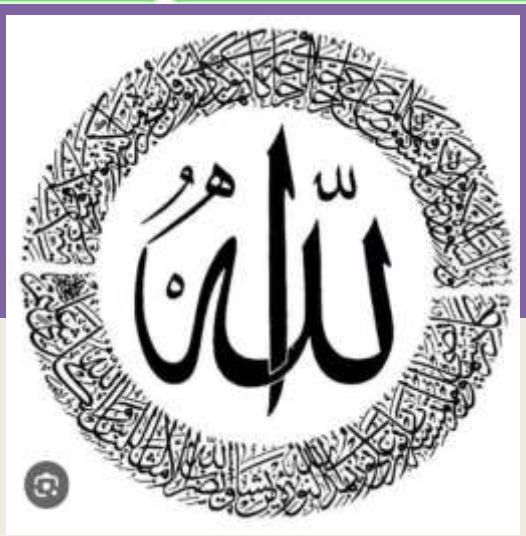

هو الله

Table 2: Summary of recent studies on pathogenesis of erythema nodosum leprosum

Study	Salient findings	Implications
Tavares *et al.*[16]	Flow cytometry of ENL patients demonstrated elevated frequency of LDN, which displayed a neutrophilic-activated phenotype Higher CD11b and lower CD62L surface expressions on LDNs correlate with the activation status of LDNs ENL patients under thalidomide treatment presented similar frequency of LDNs as observed before treatment but its activation status was lower	Potential biomarkers for diagnosis and monitoring of reactional states
Pacheco *et al.*[19]	Patients with ENL had a subpopulation of neutrophils that expressed IL-10R1 in both skin lesions and blood Neutrophils found in the blood of ENL patients were able to secrete detectable levels of TNF-α, which could be blocked by the addition of IL-10	IL-10R1 is a possible biomarker in ENL IL-10 pathway may be a therapeutic target for the management of ENL
Dias AA *et al.*[20]	DNA sensing via TLR-9 constitutes a major innate immunity pathway involved in the pathogenesis and evolution of ENL	TLR-9 antagonists are potential alternative to more effectively treat ENL
Da Silva *et al.*[18]	Abundant NETs were found in T2R skin lesions and increased spontaneous NETs formation was observed in T2R peripheral neutrophils. TLR9 expression was shown to be higher in T2R neutrophils Treatment of T2R patients with thalidomide for seven consecutive days resulted in a decrease in all of the evaluated in vivo and ex vivo NETosis parameters.	DNA recognition via TLR9 may be one of the pathways triggering this process during T2R, thus it is a potential therapeutic target
Nogueria *et al.*[22]	Compared to uninfected subjects, an increase in mature B-cells and a decrease in memory B-cells was observed in MB disease and ENL Decrease in atypical B-cells (CD27–CD21–) and an increase in activated B-cells (CD27+ CD21+) was noted during ENL episodes	First study to describe the different B-cell phenotypes in polar forms of leprosy and in ENL
Negera *et al.*[25]	Increase in activated memory B-cells and reduced number of tissue-like memory B-cells in untreated ENL patients as compared to LL patient The percentage of total circulating B-cells was similar among ENL patients and non-reactional LL patients; however, proportion of B-cells was significantly reduced by treatment for ENL	B-cell depletion may have a role in management of ENL
Da Silva *et al.*[24]	An increased density of myeloid-derived suppressor cells has been observed in patients with lepromatous leprosy and T2R Presence of annexin A1 was observed in all myeloid-derived suppressor cells. Monocytic myeloid-derived suppressor cell in the lepromatous patients had particularly higher levels of this protein when compared to the reactional patients	High annexin A1 expression in lepromatous patients may be responsible for reduction in the efficacy of T-cell action against *M. leprae*, rendering the patient susceptible to MB disease
Jesus *et al.*[26]	NGF is decreased in the course of leprosy and there is presence of autoantibodies against NGF in all clinical forms of leprosy and neuroimmune reactions Levels of autoantibodies against NGF are decreased by the immunomodulatory activity of cyclosporin A, which mainly controls pain and improves motor function and sensitivity	Suppression of anti-NGF and the regulation of NGF levels can be attractive targets for immunomodulatory treatment and for controlling the neuroimmune reactions of leprosy
Negera *et al.*[25]	Tregs in ENL maintain suppressive function despite reduced numbers Depletion of Tregs enhances TNFα and IFNγ responses, indicating a regulatory role	Tregs emerge as potential targets for immune modulation in leprosy
Castro *et al.*[13]	Decrease in CD4+TGF-β+ Treg and CD8+ TGF-β+ Treg cells Upregulation of IL-17 and IL-6	Enhances our understanding of immune hyporesponsiveness in MB patients and hyperresponsiveness in reactions
Rosa *et al.*[21]	Increased type 1 IFN expression Decreased frequency of peripheral pDC	pDC/type I IFN pathway may be utilised as potential biomarker for diagnosis Targeting pDC may be a viable therapeutic approach in ENL

B-cells: B lymphocytes, CD11b: Cluster of differentiation 11b, CD21: Cluster of differentiation 21, CD27: Cluster of differentiation 27, CD62L: Cluster of differentiation 62L, ENL: Erythema nodosum leprosum, IFN: Interferon, IL-10: Interleukin-10, IL-10R1: Interleukin-10 receptor subunit alpha, LDNs: Low-density neutrophils, MB: Multibacillary, NETs: Neutrophil extracellular traps, NGF: Nerve growth factor, pDC: Plasmacytoid dendritic cells, T2R: Type 2 reaction, TLR-9: Toll-like receptor 9, TNF-α: Tumour necrosis factor alpha

ENL patients compared to LL controls. Additionally, increased genetic expression of C1q components was noted in ENL patients' peripheral blood and skin biopsies, which normalised after treatment, suggesting C1q as a potential diagnostic marker and treatment response indicator for ENL. An immunohistochemical study also found significantly increased expression of cyclooxygenase 2 and vascular endothelial growth factor in dermal macrophages and vascular endothelium in T1Rs, followed by T2Rs, compared to controls.[43]

Pentraxin-3 (PTX-3), an inflammatory marker, is higher in MB patients before and during acute ENL and decreases within seven days of thalidomide therapy.[44] A novel study used RNA expression analysis of 1090 whole blood samples to profile 103 target genes for innate and adaptive immune

Table 3: Newer diagnostic modalities with possible role in leprosy reactions

Type of diagnostic modality	Specific investigation	Results	Role in leprosy reactions
Non-invasive imaging	Dermoscopy[35]	T1R: intense erythema, large telangiectatic vessels, violaceous to brown periappendageal pigmentation, white globules, epidermal scaling, follicular plugging T2R: erythema, vascular dilation, red dots, hypopigmented structureless areas	Diagnosis of leprosy reactions
	HRUS with colour Doppler[30]	Blood flow detected on colour Doppler in patients with nerve involvement in NCS and in those with minimal or no changes in NCS	Diagnosis of neural involvement in leprosy reactions with minimal nerve involvement or those lacking a motor response in NCS
	Magnetic resonance imaging[31–33]	Leprosy-associated peripheral nerve abscess usually reveals signal changes of an abscess with peripheral contrast enhancement of the abscess wall and inflammatory thickening of the whole nerve trunk Rarely, CNS lesions may also be diagnosed by MRI	Differentiating many mass lesions of peripheral nerves such as a schwannoma, neurofibroma and more from leprosy-associated abscess or cranial nerve involvement
Serology for *M. leprae*	Anti-PGL-1 antibody[37]	Moderate sensitivity and specificity for predicting future reactions	May predict risk of future ENL episodes, but not type 1 reaction
	Anti-NDO-LID-1 antibody[37]	Good sensitivity and specificity for predicting future reactions	
	Anti LAM salivary antibody[39]	Similar odds of predicting reaction as anti-PGL-1 antibody	
Inflammatory markers	NLR, PLR and LMR[41]	Fair sensitivity and specificity in diagnosis of leprosy reactions	Diagnosis and possibly response to anti-inflammatory therapies
	C1q[42]	Lower level during ENL, with normalization after treatment	Diagnosis of leprosy reactions and monitoring response to treatment
	Cyclooxygenase 2 and vascular endothelial growth factor expression in dermal macrophages and vascular endothelium[43]	Higher in type 1 followed by T2R compared to controls	Potential targets for treatment of lepra reactions
	Pentraxin-3[44]	Elevated prior to onset and during acute ENL, declined after treatment	Prediction of predisposition to ENL, diagnosis of ENL and monitoring response to therapy
Molecular diagnosis	Dual colour reverse-transcription multiplex ligation-dependent probe amplification[45]	A transcriptomic signature of risk for reversal reactions consisting of five genes (*CCL2, CD8A, IL2, IL15*and*MARCO*) was identified based on cross-sectional comparison of RNAexpression	Could predict reversal reactions at least two weeks before onset

Anti-LAM salivary antibody: Antibodies against lipoarabinomannan, Anti-NDO-LID-1 antibody: Anti-natural octyl disaccharide-leprosy IDRI diagnostic, Anti-PGL-1 antibody: Antibodies against Phenolic Glycolipid 1, C1q: Complement 1q, CNS: Central nervous system, ENL: Erythema nodosum leprosum, HRUS: High resolution ultrasound, LMR: Lymphocyte-to-monocyte ratio, MRI: Magnetic resonance imaging, NCSs: Nerve conduction studies, NLR: Neutrophil-to-lymphocyte ratio, Pentraxin-3: Pentraxin-related protein 3, PLR: Platelet-to-lymphocyte ratio, T1R: Type 1 reaction, T2R: Type 2 reaction

responses.[45] A transcriptomic signature of five genes (CCL2, CD8A, IL2, IL15, MARCO) was identified, predicting RRs at least two weeks before onset.[45] Other potential ENL diagnostic biomarkers include IL-6, IL-7, CCL-11, alpha-1 acid glycoprotein and CD-64.[46] No single marker or a set of markers has shown to reliably and effectively prognosticate the occurrence of lepra reactions.

The Specialist System for Evaluation of Risk of Occurrence of Reactional States in Leprosy (SEPAREH) is an online tool that predicts leprosy reactions with up to 87.7% accuracy using socio-demographic details, family history, clinical, laboratory and genetic data.[47]

Treatment

Type 1 reactions

The objective of treatment for T1R is control of neural inflammation and prevention of further immune-mediated damage. For mild T1R, non-steroidal anti-inflammatory drugs may suffice, but severe reaction, especially with neuritis, requires medical and/or surgical treatment. Current evidence suggests that oral corticosteroids are the mainstay for severe T1Rs and should be started in a dose of 0.5–1 mg/kg/day and gradually tapered to zero over a span of 20 weeks [Figure 4]. A randomised trial (Treatment of Early Neuropathy in Leprosy or TENLEP) compared oral corticosteroids for 20 and 32 weeks in patients with recent onset nerve function impairment (less than six months duration), including T1R.[48] No difference in clinical outcomes was noted between the groups at the end of the study period.

Other immunosuppressive agents that have been used successfully for the management of T1R include cyclosporine and methotrexate.[49-51]A recent review and systematic analysis has highlighted the role of methotrexate in type 1 and 2

Folder: anetoderma

0 (1).png

Box 145.3 Classification of anetoderma in children

Primary

- Isolated (±familial)
- In association with morphological abnormalities (±familial)

Secondary

- to a disorder with systemic expression (antiphospholipid syndrome, syphilis, chickenpox, HIV, other)
- to a localized pre-existing dermatosis (mastocytosis, pilomatrixomas, other)

0 (10).png

ı may be depressed,
of the subcutaneous
with an inflamma-

ıa was reported by
man with depressed
o have an atrophic,
eninger and Buzzi
c-like tumors that
ns were located on
nation[11].

ported in the world
lerma favors young
more frequently in
anetoderma reflects

CLASSIFICATION OF ANETODERMA	
Primary anetoderma	• Jadassohn–Pellizzari type: preceding inflammatory lesions • Schweninger–Buzzi type: no preceding inflammatory lesions
Secondary anetoderma	• Associated with a primary dermatosis or cutaneous tumor • Associated with a systemic disease (autoimmune, antiphospholipid syndrome, infectious) or drug
Familial anetoderma	• Both autosomal dominant and autosomal recessive forms • Usually develops in first decade of life
Anetoderma of prematurity	• Occurs in extremely premature infants • At sites of monitoring leads or adhesives

Table 99.2 Classification of anetoderma.

the presence or absence of clinical inflammation at the onset of the

0 (11).png

e chest, back,
y develops in
r many years

trophic lesion
lesion. Some
lying disease
autoimmune
instance, the
nown inflam-
id antibodies
etoderma are
ieterogeneous
lined in Table
:], the clinical

re infants. In
ous monitor-
6.
malities have
cardiac, pul-
been no con-
y are probably
may reflect a
efined.

nis of affected
n present but
The majority

ssue stains) is
papillary and/
ormal, irregu-
ls and histio-

or granular
the dermal–
s in affected
cally.
and irregular

SECONDARY ANETODERMA – ASSOCIATED CONDITIONS	
Infectious	• Varicella • Folliculitis • Syphilis (cutaneous) • Lepromatous leprosy • Molluscum contagiosum • Tuberculosis (cutaneous) • HIV infection • Acrodermatitis chronica atrophicans • Post-hepatitis B immunization
Drugs	• Penicillamine
Inflammatory	• Acne vulgaris • Mastocytosis • Lichen planus • Granuloma annulare • Juvenile xanthogranuloma • Cutaneous sarcoidosis • Cutaneous lymphoid hyperplasia (lymphocytoma cutis) • Prurigo nodularis • Insect bites
Autoimmune	• Discoid and systemic lupus erythematosus • Antiphospholipid syndrome • Primary Sjögren syndrome • Addison disease • Graves disease
Tumors and depositions	• Involuted infantile hemangioma • Pilomatricoma • Melanocytic nevus • Dermatofibroma • Dermatofibrosarcoma protuberans • Primary cutaneous marginal zone B-cell lymphoma (formerly primary cutaneous plasmacytoma or immunocytoma) • Mycosis fungoides • Nodular amyloidosis • Xanthoma

Table 99.3 Secondary anetoderma – associated conditions.

0 (2).png

Box 145.4 Morphological abnormalities described with anetoderma

Eye abnormalities

- Cataract
- Keratoconus
- Corneal opacities
- Optic atrophy (secondary to bony changes)

Cardiovascular abnormalities

- Mitral valve prolapse
- Aortic insufficiency
- Wolff–Parkinson–White

Osteoarticular abnormalities

- Abnormal calcifications
- Kyphoscoliosis
- Shortening of a limb
- Congenital fusion of cervical vertebrae
- Spina bifida
- Osteopetrosis
- Metaphyseal dysplasia
- Hip dislocation

Miscellaneous

- Emphysema
- Protrusion of teeth
- Pyramidal syndrome
- Myotonic dystrophy
- Diverticulum of midoesophagus
- Blegvad–Haxthausen syndrome
- (anetoderma, osteogenesis imperfecta)

0 (3).png

Box 145.5 Differential diagnosis of anetodermic lesions

- Chickenpox scars
- Papular acne scars
- Lichen sclerosus et atrophicus (LSA)
- Atrophoderma of Pasini and Pierini
- Perifollicular macular atrophy
- Atrophoderma vermiculare
- Acquired cutis laxa
- Striae distensae
- Connective tissue naevus
- Neurofibromas
- Piezogenic papules
- Focal dermal hypoplasia (Goltz)

0 (4).png

Box 94.1 Selected acquired forms of cutaneous atrophy

- Generalised cutaneous thinning:
  - Ageing (see earlier in this chapter)
  - Rheumatoid disease (Chapter 155)
  - Glucocorticoids (exogenous or endogenous)
- Acquired poikiloderma
- Striae
- Atrophic scars:
  - Stellate pseudoscars
- Spontaneous atrophic scarring of the cheeks
- Acrodermatitis chronica atrophicans (Lyme borreliosis)
- Atrophodermas:
  - Follicular atrophoderma
  - Linear atrophoderma (Moulin)
  - Atrophoderma of Pasini and Pierini
- Paroxysmal haematoma of the finger (Achenbach syndrome)
- Panatrophy:
  - Local panatrophy
  - Facial hemiatrophy

Figu
a yo

Pat
Pre
Ste

(Box 114.2). Some are covered elsewhere in this chapter.

Box 114.2 Causes of atrophic lesions in neonates

- Morphoea
- Atrophic dermatofibrosarcoma protuberans
- Cutis marmorata telangiectatica congenita
- Aplasia cutis congenita
- Anetoderma of prematurity
- Congenital erosive and vesicular dermatosis healing with reticulated supple scarring
- Medallion-like dermal dendrocyte hamartoma
- Congenital infection (HSV and VZV; may be zosteriform)
- Focal dermal hypoplasia of Goltz
- Neonatal lupus erythematosus

HSV, herpes simplex virus; VZV, varicella zoster virus.

0 (6).png

ıe acetonide
uma) cream,
in an open-
skin atrophy
twice weekly

/ice daily has
intralesional
ıangioma.[144]
be effective
l TCS sprays
e peristomal
ostomy bag

tly from the
hese AE and

ary–Adrenal
ıtaneously in
l to those of
A axis, iatro-
infants and

- Delayed wound healing

• BOX 45.6 Risk Factors for Systemic Effects and Local Atrophy

Systemic Effects

- Young age (infancy/childhood)
- Liver disease
- Renal disease
- Amount of topical corticosteroid (TCS) applied
- Potency of TCS
- Use of occlusion
- Lack of physician supervision

Local Atrophy

- Young age (infancy/childhood)
- Potency of TCS
- Use of occlusion
- Location (face, neck, axilla, groin, and upper inner thighs)

paralleled increases in circulating leukocytes.[154] Normal and psoriatic or eczematous adult volunteers applying more than 50 g of

0 (7).png

Box 65-1

Differential Diagnosis of Primary Anetoderma

ELEVATED	DEPRESSED
Secondary anetoderma	Secondary anetoderma
Acne scars	Glucocorticoid-induced atrophy
Keloids	Acne scars
Nevus lipomatosus superficialis	
Papular elastorrhexis	
Connective tissue nevi	

ogy demonstrates focal degeneration of elastic fibers and normal collagen. There are no associated extra-cutaneous abnor-

0 (8).png

TABLE 70-1

Conditions Associated with Secondary Anetoderma

Infectious
- Syphilis
- Lyme disease
- Leprosy
- Molluscum contagiosum

Inflammatory
- Granuloma annulare
- Discoid lupus erythematosus
- Sarcoidosis
- Lichen planus

Tumoral
- Pilomatricomas
- Juvenile xanthogranuloma
- Xanthomas
- Involuted infantile hemangiomas
- Cutaneous B-cell lymphoma

Other Conditions[a]
- Antiphospholipid syndrome
- Autoimmune thyroiditis
- HIV

[a]Also associated with primary anetoderma.

also has been described in premature infants, possi-

ectopic mature lipocytes located in the dermis.

TABLE 70-2
Differential Diagnosis of Primary Anetoderma

ELEVATED	DEPRESSED
Secondary anetoderma	Secondary anetoderma
Acne scars	Glucocorticoid-induced atrophy
Keloids	Acne scars
Nevus lipomatosus superficialis	
Papular elastorrhexis	
Connective tissue nevi	

case of
elastic tis
have beer
white wo

PATHO

The pathe
eration is
been pos
the deger
sunlight a
Other pos
thesis of

Figure 3: (a) Multiple well-defined erythematous nodules (black circle) over the chest and abdomen. Two, well-defined, round to oval, circumscribed atrophic plaques (black arrow) with a wrinkled appearance around the left nipple region. (b) Anetoderma lesion flattened on stretching and returned to its original texture when left loose (black arrow)

of the anetoderma lesion showed homogenous white and yellow areas with distended skin markings [Figure 4c]. The patient was started on oral prednisolone (0.75 mg/kg/day), which was tapered over 12 weeks.

Clinically, anetodermas manifest as clusters of circular or oval pink macules or plaques, typically ranging from 0.5 cm to 1 cm in diameter. Over time, these skin lesions gradually fade and flatten from the center outwards, leaving behind atrophic macules that are depressible under pressure.[1,2] The various causes of anetoderma are mentioned in Table 1.[1-4]

In leprosy patients, the arrangement of elastic fibers may become irregular, sometimes fragmented, and locally aggregated.[5] There are limited reports of lepromatous leprosy leading to secondary anetoderma.[1,6-8] In leprosy, inflammatory cells instigate changes in the dermis, replacing the normal dense matrix with a looser one more conducive to ongoing inflammation. This transformation primarily involves neocollagenesis, collagenolysis, elastolysis, and proteoglycan degradation.[6] Macrophages within the lesions of lepromatous leprosy may produce elastolysis enzymes, while neutrophils recruited during lepra reactions can contribute to elastolysis.[7]

Elastolysis in leprosy, particularly prevalent in sun-exposed areas, can clinically resemble annular elastolytic giant cell granuloma.[6] Generalized anetoderma has been observed in an HIV-positive man co-infected with leprosy and tuberculosis.[2] Once elastic tissue is lost, it cannot be fully regenerated during the recovery process, making anetoderma resulting from elastolysis a long-term complication of leprosy.[6]

Diagnosis primarily relies on clinical examination, and can be confirmed through skin biopsy. Special staining methods, such as Verhoff-Van Gieson or orcein staining, are necessary to identify elastic fibers, elastolysis, and elastorrhexis in the dermis.[1,2] Anetodermas have a chronic course, and are highly resistant to treatment. A combination of a 595 nm pulsed-dye laser with a 1550 nm non-ablative fractionated laser may offer clinical improvement by stimulating elastogenesis and reducing fiber fragmentation.[8]

Table 1: Causes of anetoderma

Primary anetoderma
• Jadassohn-Pellizzari type
• Schwninger-Buzzi type
Secondary anetoderma
Infections
• Tuberculosis
• Leprosy
• Pityriasis versicolor
• Syphilis
• Lyme disease
• Molluscum contagiosum
• HIV-1 disease
• Varicella zoster
Inflammatory dermatoses
• Acne vulgaris
• Sarcoidosis
• Urticaria pigmentosa
• Granuloma annulare
• Prurigo nodularis
Autoimmune conditions
• Systemic lupus erythematosus
• Sjogren's syndrome
• Grave's disease
• Addison's disease
• Antiphospholipid syndrome
• Autoimmune haemolytic anemia
Cutaneous malignancies
• Cutaneous B-cell lymphomas
• Cutaneous T-cell lymphomas
Adnexal tumors
• Pilomatrixoma
• Myxofibrosarcoma
Deposition disorder
• Xanthomas
• Nodular amyloidosis
Miscellaneous
• Post-hepatitis-B vaccination
• Hamartomatous congenital melanocytic nevi
• Penicillamine-induced anetoderma
• Anetoderma of prematurity
• Familial anetoderma

Folder: demodex mites

0 (1).png

Table 3: Common therapeutic modalities for demodicosis.

Topical treatment (6–8 weeks)	Systemic treatment
• Metronidazole 2% • Permethrin 5% • Crotamiton • Gamma benzene hexachloride • Benzyl benzoate • Sulphur • 1% Ivermectin • Combination therapies	• Metronidazole 250 mg thrice for 2 weeks • Ivermectin 200 mcg/kg, 2 doses a week apart • Doxycycline • Isotretinoin

neurotoxic effects on Demodex mites, continues to be one of

0 (157).png

Table 10.2 Differential diagnosis of Demodex folliculitis

Condition	Clinical features	Dermoscopy	Histopathology
Demodex folliculitis	Diffuse facial erythema, follicular plugs and vesiculopustular, which impart a 'nutmeg grater' appearance to the skin	Demodex tails, filaments protruding out of follicular openings and erythema and scales	Follicular infundibulum contains multiple Demodex mites with perifollicular lymphohistiocytic inflammation
Seborrheic dermatitis	Yellowish greasy scaling with erythema.	Patchy distribution of dotted vessels, fine yellow scales over an erythematous background	Parakeratosis, follicular plugging, spongiosis, lymphocytic exocytosis, tortuous blood vessels
Erythemato-telangiectatic rosacea	Presence of telangiectasia with burning and stinging sensation associated with papules and pustules	Linear tortuous vessels with large polygons. Patulous follicular opening with plugs and scaling seen	Dilated capillaries in the upper dermis

Table 12.1 Primary human demodicosis: proposed classification and nomenclature

Proposed nomenclature	Definition and clinical manifestations
Spinulate demodicosis	Discrete fine, whitish to yellowish, spiky, changes involving sebaceous hair follicles, with or without faint erythema and little inflammation
Papulopustular demodicosis, perioral demodicosis, periorbital demodicosis, periauricular demodicosis	Papulopustules mostly involving the face (predilection for perioral, periorbital, and periauricular regions), in patients without (primary form) or with preexisting inflammatory dermatoses (secondary form)
Nodulocystic/ conglobate demodicosis	Intense immune reaction with massive follicular and perifollicular inflammatory infiltrates caused by *Demodex* proliferation, pus accumulation, and suppurative succulent changes

Adapted from Chen et al. [16]

0 (3).png

Table 27.7 *Demodex*

	D. FOLLICULORUM	*D. BREVIS*
Ovum (length × width)[a]	105 × 42	60 × 34
Larva (length × width)	283 × 34	105 × 34
Protonymph (length × width)	365 × 36	148 × 34
Nymph (length × width)	392 × 42	165 × 41
Male adult		
Length	280	166
Width	24–45	17–46
Female adult		
Length	294	208
Width	27–52	19–50
Male to female ratio	1:4.5	1:3.4
Habitat	Hair follicle	Sebaceous gland

[a]Measurements of all sizes in mm. From Desch and Nutting (1972).[193]

The n
seem to
lowest i
host, re
reporte
with a r
tion rat
28.5 ye
low seb
Demode
Infest
During
skin sur
of adul
abdome
with a r
in the
account
reporte

DEMO

Two to
conside
can elic

0 (34).png

TABLE 2.6.7 OTHER MITES OF SIGNIFICANCE

Mite	Disease(s) Associated
Acarus (grain mite)	Baker's itch
Liponyssoides sanguineus (house mouse mite)	Transmits rickettsialpox
Cheyletiella	Walking dandruff in pets. May cause papules and vesicles in humans
Demodex folliculorum	Rosacea, blepharitis, HIV folliculitis Treatment: Permethrin
Dermatophagoides (house dust mite)	Allergic reactions
Glycyphagus (cheese mite)	Grocer's itch
Leptotrombidium (Trombicula)	Dermatitis; can transmit scrub typhus
Trombicula alfreddugesi (chigger mite/red bug)	Chigger bites Summer penile syndrome in children

0 (4).png

Table 2: When to suspect primary and secondary demodicosis.

Primary demodicosis	Secondary demodicosis
Late onset, >40 years	Can occur early in life
Facial involvement (perioral, periocular, periauricular)	Can have truncal involvement also
Asymmetric distribution, grouped in an irregular shape with satellite lesions within one affected area	More diffuse and symmetrical involvement
Follicle centric	
Asymptomatic/mildly pruritic	More extensive inflammation hence symptoms
Lack of classical manifestations of rosacea like erythema, flushing, or telangiectasia	Past history and features of underlying disease such as perioral dermatitis and rosacea are evident

TABLE 208-1
Mites

TYPE OF MITE	SCIENTIFIC NAME	CLINICAL FEATURES—DISEASE ASSOCIATIONS
Scabies mites	*Sarcoptes scabei*	See the section Scabies
Follicle mites	*Demodex folliculorum hominis* and *D. brevis*	Questionable association with rosacea, idiopathic facial burning
Food mites	Grain mite: *Acarus siro* Cheese mite: *Tyrolichus casei* Grocery mite: *Tyrophagus putrescentiae*	Mild dermatitis known as *baker's itch* or *grocer's itch*
Fowl mites	*Dermanyssus gallinae* and *D. avium*	Pruritic papules, sometimes with a hemorrhagic center
Straw itch mites	*Pyemotes tritici* and *P. ventricosus*	Patchy dermatitis on trunk and arms during or after harvesting
Harvest or red mites (chiggers)	Genus *Trombicula* *Eurotrombicula alfreddugesi* and *E. splendidus* most common in United States	Scrub typhus vector (*Leptotrombidium* sp.) Papular to vesicular lesion found on ankles, waist, or warm skinfolds
Animal mites	*Ornithonyssus bacoti* *Liponyssoides sanguineus* *Cheyletiella* "walking dandruff"	Endemic/murine typhus vector Rickettsialpox vector Non-specific, pruritic eruption on body parts in close contact with infested pets
House dust mites	*Dermatophagoides* sp.	Questionable association with atopic dermatitis

0 (7).png

Table 33.1 Mites of medical importance

MITES	DISEASE
Acarus (grain mite)	Baker's itch
Glycyphagus (cheese mite)	Grocer's itch
Dermanyssus and *Ornithonyssus* (fowl mite)	Equine encephalitis
Liponyssoides sanguineus (house mouse mite)	Rickettsial pox
Dermatophagoides (dust mite)	Allergy
Trombicula (chigger mite)	Scrub typhus
Demodex spp.	Folliculitis, possibly rosacea

Bolognia JL, Jorizzo JL, Schaffer JV. Dermatology. *Madrid, Spain: Elsevier Saunders; 2012: Chapter 85.*

0.png

Table 4-23: Select Mites *(Figure 4.45A)*

Mite	Common Name	Disease
Acarus siro	Grain mite (found in hay, grain and house dust)	Baker's itch
Allodermanyssus (Liponyssoides) sanguineus	House mouse mite	Rickettsialpox
Cheyletiella		Walking dandruff (cats, dogs, rabbits)
Dermanyssus gallinae	Fowl mite	Equine encephalitis
Dermatophagoides farinae	Dust mite	Allergic reaction
Glyciphagus domesticus	Cheese mite Grocer's mite (found in cheese, grains, hay, mattress)	Grocer's itch
Laelaps, Androlaelaps, Eulaelaps	Rodent mites	Murine typhus, tularemia, spotted fever
Pyemotes ventricosus	Straw itch mite	
Trombicula alfreddugesi	Chigger mite	Bites (group pruritic vesicles/papules on lower legs) – larva attaches to host and drop off after feeding

mite (1).png

MITE FAMILIES	
Acaridae	Food mites
Demodicidae	Follicle mites
Dermanyssidae	Bird, rodent mites
Glycyphagidae	Food mites
Haemoganasidae	Straw mites
Psoroptidae	Mange, scab mites
Pyemotidae	Grain mites, straw mites
Sarcoptidae	Scabies mites
Trombiculidae	Chigger, harvest mites

Table 85.5 Mite families.

MITES OF MEDICAL IMPORTANCE

mite (2).png

se dust

apan)

cea, blepharitis;
gs and cats

irds, rodents,

lankets,
tored foods

eactions with

ocer's mite:
sses

PREPARATION OF COLLECTED MITES FOR MICROSCOPIC EXAMINATION
Preferred method
• Clear with either lactic acid or lactophenol (may take hours to days) • Wash with water • Mount in Hoyer's medium*
Rapid method
• Mount live or alcohol-fixed mites directly in Hoyer's medium* • Mount live mites in Permount™ (details of mites less obvious)
*Prepared by adding 30 g of gum Arabic to 50 ml distilled water, then adding 200 g chloral hydrate followed by 20 g glycerin; filter through cheesecloth.

Table 85.7 Preparation of collected mites for microscopic examination. If mites are collected onto filters inside a vacuum cleaner, the filter samples are treated with potassium hydroxide (KOH) and then floated in concentrated sugar solution to collect the mites.

rickettsial disease, and serologic testing can be helpful. As with tick-borne rickettsial diseases, biopsy of the eschar can be sent for immunohistochemical staining or PCR to distinguish typhus group organisms

MITE FAMILIES	
Acaridae	Food mites
Demodicidae	Follicle mites
Dermanyssidae	Bird, rodent mites
Glycyphagidae	Food mites
Haemoganasidae	Straw mites
Psoroptidae	Mange, scab mites
Pyemotidae	Grain mites, straw mites
Sarcoptidae	Scabies mites
Trombiculidae	Chigger, harvest mites

Table 85.5 Mite families.

MITES OF MEDICAL IMPORTANCE	
Acarus siro	Grain mite: hay, grain, house dust
	Baker's itch
Cheyletiella spp.	**Walking dandruff on pets**
Cheyletus malaccensis	Wheat mite
	Wheat warehouse itch (Japan)
Demodex spp.	**Folliculitis; possibly rosacea, blepharitis; demodectic mange in dogs and cats**
Dermanyssus gallinae, D. avium	Fowl mite: chickens, wild birds, rodents, rabbits
Dermatophagoides farinae, D. pteronyssinus	Dust mite (**allergy**): dust, blankets, mattresses, pillows, pets, stored foods and grains
Euroglyphus maynei	Dust mite (**allergy, cross-reactions with other dust mites**)
Glycyphagus domesticus	Cheese mite, barn mite, grocer's mite: cheese, grains, hay, mattresses
	Grocer's itch
Laelaps spp., *Androlaelaps* spp., *Eulaelaps* spp.	Rodent mites
Lepidoglyphus destructor	Dust mite, hay mite
Liponyssoides (Allodermanyssus) sanguineus	House mouse mite
	Rickettsialpox
Neotrombicula autumnalis	Harvest mite (Northern Europe)
Ophionyssus natricus	Snake mite
Ornithonyssus sylviarum, O. bacoti, O. bursa	Tropical rat mite, fowl mite, tropical fowl mite, northern fowl mite: rodents, chickens, wild birds, carnivores
Pyemotes ventricosus, P. tritici	Straw itch mite, grain mite: parasites of insects in grains and straw
Trombicula (Eutrombicula) alfreddugesi	Chigger mite, red bug
Trombicula (Leptotrombidium) akamushi, L. deliense, L. fletcheri, L. arenicola, L. pallidum, L. pavlovskyi, L. scutellare	Scrub mite
	Scrub typhus
Tyrophagus putrescentiae	Mold mite, grain storage mite
	Copra itch

Table 85.6 Mites of medical importance. Scientific names, common names and associated diseases (in **bold**) are listed. With the exception of *Demodex* and dust mites, mite bites typically lead to pruritic papular eruptions in humans.

Fig. 85.14 Avian mite bites. Multiple erythematous pruritic papules, several of which have hemorrhagic crusts. The exposure was birds nesting on the patient's house. *Courtesy, Jean L Bolognia, MD.*

PREPARATION OF COLLECTED MITES FOR MICROSCOPIC EXAMINATION
Preferred method
• Clear with either lactic acid or lactophenol (may take hours to days) • Wash with water • Mount in Hoyer's medium*
Rapid method
• Mount live or alcohol-fixed mites directly in Hoyer's medium* • Mount live mites in Permount™ (details of mites less obvious)
*Prepared by adding 30 g of gum Arabic to 50 ml distilled water, then adding 200 g chloral hydrate followed by 20 g glycerin; filter through cheesecloth.

Table 85.7 Preparation of collected mites for microscopic examination. If mites are collected onto filters inside a vacuum cleaner, the filter samples are treated with potassium hydroxide (KOH) and then floated in concentrated sugar solution to collect the mites.

rickettsial disease, and serologic testing can be helpful. As with tick-borne rickettsial diseases, biopsy of the eschar can be sent for immunohistochemical staining or PCR to distinguish typhus group organisms from the spotted fever group.

Differential diagnosis

Mite-induced dermatoses are often misdiagnosed. Bullous lesions are especially common, and false-positive direct immunofluorescence has been described. Histologic features resembling those of an insect bite may suggest the correct diagnosis, as may a clinical pattern of skin lesions corresponding to areas of exposure. However, eosinophil-rich subepidermal bullae occur in both mite infestation and bullous pemphigoid, so a careful history is essential.

Mite-induced dermatitis can be associated with pets, rodents, straw bedding, bird nests, grains, and even onion bulbs (see Table 85.6). Avian mite dermatitis may also be associated with pet rodents, such as gerbils. Pets should be examined by a knowledgeable veterinarian; skin scraping, adhesive tape stripping, or biopsy may reveal the mite(s) on the animal. Vacuum cleaners can also be fitted with filters to collect mites (Table 85.7). Another helpful technique is to spray areas of dandruff or crust on a pet with an acaricidal agent recommended by a veterinarian. A fine-toothed comb or toothbrush is then used to remove the scale-crust, which is placed in a sealed bag. When alcohol is added to the bag, scale-crust and hair will sink, whereas mites will float.

Treatment

Some types of mites inflict a "bite and run" injury, while others remain attached for a prolonged meal. Scraping, tape stripping, or vigorous washing with soap and water are all effective in removing or killing

Insect repellents containing diethyltoluamide (DEET) offer the most effective protection against mosquitoes, flies, fleas, mites, and ticks. Ethyl hexanediol, dimethyl phthalate, and dimethyl carbate butopyronoxyl provide a narrower spectrum of prevention compared with DEET. Use of a combination of these repellants improves effectiveness. Repellants form a barrier against penetration that extends <4 cm away from the skin. DEET also blocks the mosquitoes ability to track human carbon dioxide vapor trails. Repellants do not mask other insect stimuli such as sweat, moisture, and warmth. DEET protection lasts about 10 to 12 hours at room temperature, but can be shortened by clothing friction, water, sweat, wind, or heat. Repellants may last several days on fabrics. Mosquito nets and clothing should also be used in areas where mosquitoes serve as vectors for disease.

MITES

I. BACKGROUND Mites are a form of arachnid that parasitize humans and feed on organic matter. Depending on the type of mite, a range of dermatologic manifestations are seen.

II. CLINICAL PRESENTATION Mite infestations manifest as papulosquamous, urticarial, inflammatory, or even bullous dermatoses. They are also responsible for transmitting infectious diseases. Clinical manifestations and diseases associated with specific mites are outlined in Table 6-6. Cheyletiella mites eat keratin on small mammals, giving dogs and cats "walking dandruff."

TABLE 6-6 Mite-Associated Disease

Mite	Associated Disease	Treatment
Acarus (grain mite)	Baker itch	Pest control Symptomatic relief[a]
Allodermanyssus sanguineus (house mouse mite)	Rickettsial pox	Doxycycline[b]
Cheyletiella	Walking dandruff	Treat pets: - Ectoparasitic shampoos and dips) - Permethrin spray - Fipronil spray - Topical amitraz Symptomatic relief[a]
Demodex	Rosacea	Topical sulfur (initial treatment) Other topicals: - Permethrin 5% - Salicylic acid

(*Continued*)

(c) 2015 Wolters Kluwer. All Rights Reserved.

TABLE 6-6 Mite-Associated Disease (Continued)

		- Metronidazole - Crotamiton - Lindane - Retinoids Oral ivermectin Oral retinoids
Dermanyssus (fowl mite) *Ornithonyssus* (fowl mite)	Equine encephalitis Western equine encephalitis	Removal of infested birds and nests House cleaning and fumigation Symptomatic relief[a] Topical acaricides - Gamma benzene hexachloride 1% - Crotamiton - Permethrin - Malathion
Dermatophagoides (dust mite)	Allergic reactions Atopic dermatitis	Humidity < 50% Mattress and pillow protective coverings Wash bedding once weekly in hot water Symptomatic relief[a]
Glycyphagus (cheese mite)	Grocer itch	Pest control Symptomatic relief[a]
Sarcoptes scabei (scabies mite)	Pruritic dermatitis	Wash clothes and bedding in hot water Pest control Topical permethrin Oral ivermectin
Trombicula (chigger mite)	Dermatitis and scrub typhus	Symptomatic relief,[a] additionally: - Antipruritics: camphor, menthol - Topical anesthetics with pramoxine - Potent topical corticosteroids under occlusion - Ice application - Excision of refractory lesions

[a]Symptomatic relief for mite-associated dermatitis includes topical corticosteroids and oral antihistamines. [b]Antibiotics may shorten the duration of symptoms. Second-line antibiotics include erythromycin, tetracycline, and chloramphenicol.

(c) 2015 Wolters Kluwer. All Rights Reserved.

Table 4-9: Non-Venereal Treponemal Infections

Disease	Organism/Transmission	Clinical Findings
Yaws (Frambesia)	***Treponema pallidum*** (subspecies ***pertenue***) Transmission: direct contact with infectious lesions	– Primary: one to few erythematous papules at inoculation site ('mother yaw') usually on lower leg of child → enlarges, ulcerates and disappears with resultant scar – Secondary: smaller 'daughter yaws' lesions spread symmetrically over body – Tertiary: skin and skeletal changes (no CNS or cardiovascular problems): gummata, keratoderma, midfacial destruction, bony inflammation and damage, nodular lesions Of note, mucosal yaws appear similar to condyloma lata
Pinta (Carate)	***Treponema carateum*** Transmission: direct contact with infectious lesions (± possible insect vectors)	– Primary: smooth papule at inoculation site – Secondary: small psoriasiform yellowish-brown papules and plaques (pintids) – Tertiary: depigmented vitiligo-like lesions over face, wrists, trochanteric areas
Endemic syphilis (Bejel)	***Treponema pallidum*** (subspecies ***endemicum***) Transmission: direct skin contact	– Primary: skin lesions rare – Secondary: mucosal lesions including mucous patches, condylomata lata, and lymphadenopathy, ± osteitis, periostitis, bony damage, gummata (CNS and cardiovascular problems very rare)
Treatment for venereal and non-venereal treponematoses: 2.4 million units of **benzathine PCN** If PCN-allergic, can use doxycycline in same dosage as for venereal syphilis		

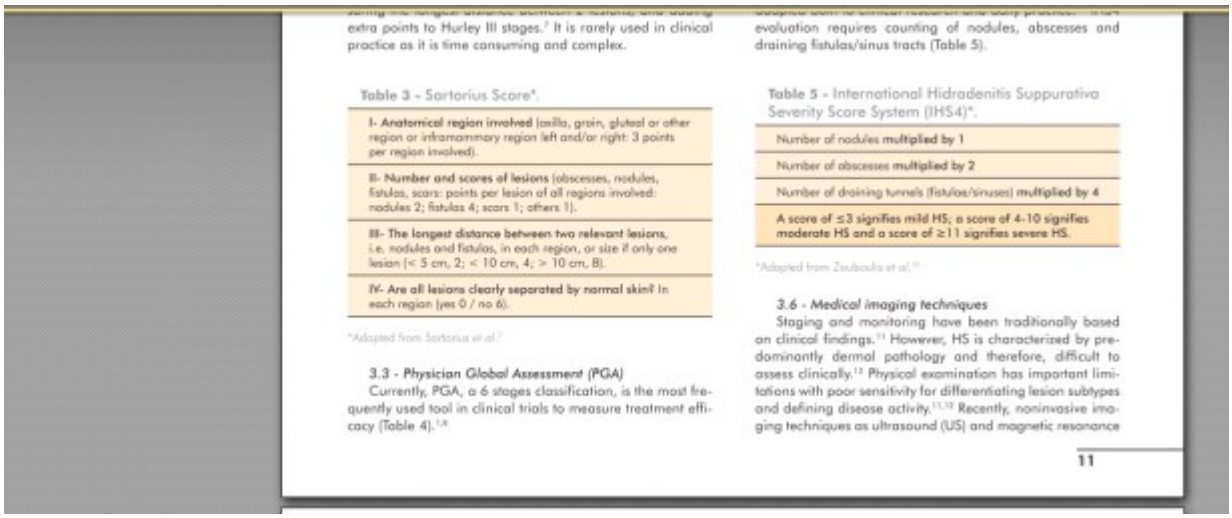
Syphilis (Lues, Venereal Syphilis) *(Figure 4.17, 4.18A-C)*

- Chronic systemic infection caused by *Treponema pallidum* (subsp. *pallidum)*, involving multiple organs including skin, cardiac, neurologic and skeletal system
- Transmission can be sexual (contact with infectious lesion), transplacental or from blood products (rare)
- Clinical stages divided as follows:
- **Primary stage**
  - Chancre: localized infection at inoculation site presenting as highly infectious, indurated, painless erosion or ulceration; spontaneous resolution within 1-2 months, ± regional lymph node enlargement

Figure 4.17:
Primary syphilis
(Courtesy of Dr. Paul Getz)

Folder: hidradenitis

0 (1).png



extra points to Hurley III stages.[7] It is rarely used in clinical practice as it is time consuming and complex.

Table 3 - Sartorius Score*.

I- Anatomical region involved (axilla, groin, gluteal or other region or inframammary region left and/or right: 3 points per region involved).
II- Number and scores of lesions (abscesses, nodules, fistulas, scars: points per lesion of all regions involved: nodules 2; fistulas 4; scars 1; others 1).
III- The longest distance between two relevant lesions, i.e. nodules and fistulas, in each region, or size if only one lesion (< 5 cm, 2; < 10 cm, 4; > 10 cm, 8).
IV- Are all lesions clearly separated by normal skin? In each region (yes 0 / no 6).

*Adapted from Sartorius et al.[7]

3.3 - *Physician Global Assessment (PGA)*

Currently, PGA, a 6 stages classification, is the most frequently used tool in clinical trials to measure treatment efficacy (Table 4).[1,8]

evaluation requires counting of nodules, abscesses and draining fistulas/sinus tracts (Table 5).

Table 5 - International Hidradenitis Suppurativa Severity Score System (IHS4)*.

Number of nodules **multiplied by 1**
Number of abscesses **multiplied by 2**
Number of draining tunnels (Fistulas/sinuses) **multiplied by 4**
A score of ≤3 signifies mild HS; a score of 4-10 signifies moderate HS and a score of ≥11 signifies severe HS.

*Adapted from Zouboulis et al.[11]

3.6 - *Medical imaging techniques*

Staging and monitoring have been traditionally based on clinical findings.[11] However, HS is characterized by predominantly dermal pathology and therefore, difficult to assess clinically.[12] Physical examination has important limitations with poor sensitivity for differentiating lesion subtypes and defining disease activity.[11,13] Recently, noninvasive imaging techniques as ultrasound (US) and magnetic resonance

0 (10).png

Table 3.1 HS cutaneous findings

HS cutaneous lesions			
		Typical	Other
Primary	**Secondary**	**Tertiary**	
Nodules[a]	Sinus tracts[b]	Double-ended pseudocomedones[d]	Follicular papules/pustules
Abscesses[a]	Drainage sinuses[b]	Scars (hypertrophic scars/keloids, bridle[c], rope/cord-like and atrophic scars)	Epidermal cysts

[a]Nodules with different depths.
[b]Tunnels.
[c]Cords.
[d]Interconnected keratin-filled multipores.

0 (11).png

Table 5.1 Hurley staging system

Stage	Abscesses	Sinus tracts	Cicatrization
I	Single or multiple	–	–
II	Recurrent (separated)	+ (separated)	+
III	+++	Multiple, interconnected	++

Hidradenitis Suppurativa: A Diagnostic Atlas, First Edition. Giuseppe Micali.
© 2017 John Wiley & Sons Ltd. Published 2017 by John Wiley & Sons Ltd.

0 (12).png

Table 5.2 HS-PGA scale

Stage	Description
1	Clear, no inflammatory or non-inflammatory nodules
2	Minimal, only the presence of non-inflammatory nodules
3	Mild, less than five inflammatory nodules or one abscess or draining fistula and no inflammatory nodules
4	Moderate, less than five inflammatory nodules or one abscess or draining fistula and one or more inflammatory nodules or two to five abscesses or draining fistulas and less than ten inflammatory nodules
5	Severe, two to five abscesses or draining fistulas and ten or more inflammatory nodules
6	Very severe, more than five abscesses or draining fistulas

and fistulas) within seven anatomical regions (left axilla, right axilla, left groin, right groin, left buttock region, right buttock

0 (13).png

Table 5.4 Hidradenitis Suppurativa Latent Class analysis by Canoui-Poitrine *et al.* [9]. Reproduced with permission of Elsevier

	Type 1 Axillary-mammary	Type 2 Follicular	Type 3 Gluteal
Gender	F >> M	M >> F	F > M
Locations	Breast and/or armpit	Breast and/or armpit, ears, chest, back, and/or legs	Gluteal region (predominant)
Type of lesions	Hypertrophic scars	Follicular lesions (comedones, epidermal cysts, sinus pilonidalis)	Follicular papules and folliculitis
HS family history	Common	More common	Common
Disease severity	More severe than LC3 but less severe than LC2	Highest severity	Lowest severity
Disease duration	Lowest duration	Highest duration	Between LC1 and L2
Past or current smoking history	Less frequent than LC2 and LC3	Comparable to LC3	Comparable to LC2
Past or actual acne history	Medium rate	Highest rate	Lowest rate
Overweight or obesity	Comparable to LC2	Comparable to LC1	Less common

0 (14).png

	Clinical features									
Acronym	Psoriatic arthritis	Pyogenic arthritis	Pyoderma gangrenosum	Acne	HS	Ankylosing spondylitis	Synovitis	Pustulosis	Hyperostosis	Osteitis
PASH	–	–	+	+	+	–	–	–	–	–
PsAPASH	+	–	+	+	+	–	–	–	–	–
PAPASH	–	+	+	+	+	–	–	–	–	–
PASS	–	–	+	+	+	+	–	–	–	–
SAPHO	–	–	–	+	+/–	–	+	+	+	+

Table 7.3 Acronyms and clinical features of follicular occlusion syndromes with HS

	Clinical features			
Syndromes	Acne conglobata	HS	Dissecting cellulitis of the scalp	Pilonidal cyst
Follicular occlusion triad	+	+	+	–
Follicular occlusion tetrad	+	+	+	+

neously or develop as a consequence of HS surgical treatments. Superimposed infections may extend deeply in the and of the consequent blockade/destruction of lymph drainage routes. A subtle, subclinical condition of lymphedema,

Table 8.1 Complications in HS

Local	Regional	Systemic
Superimposed infections	Sacral bacterial osteomyelitis	Sepsis/septicemia
Cellulitis	Lumbosacral epidural abscess	Oral and liver malignancies
Scarring	Urethral, bladder, rectal, or peritoneal fistulas	Arthropathy
Anal/perianal fistulas	Retraction and reduction of limb mobility	Anemia
Anal, rectal, preputial, urethral strictures		Polyclonal gammopathy
Penile degloving		Hypoproteinaemia
Lymph nodes enlargement		Amyloidosis
Lymphedema		Malaise
Lymphangiectasias		Depression, suicide ideation
Massive genital edema		
Scrotal elephantiasis		
Lichen simplex chronicus		
Squamous cell carcinoma		

Hidradenitis Suppurativa: A Diagnostic Atlas, First Edition. Giuseppe Micali.
© 2017 John Wiley & Sons Ltd. Published 2017 by John Wiley & Sons Ltd.

0 (16).png

Table 9.3 Elementary lesions in the HS setting

Type	Definition
Pseudocyst (nodule) (Figure 9.3)	Round- or oval-shaped hypoechoic or anechoic nodular dermal and/or hypodermal structure (usually ≤ 1 cm) (Figure 9.4)
Fluid collection (abscess) (Figure 9.5)	Hypoechoic or anechoic fluid dermal and/or hypodermal deposits connected to the base of widened hair follicles (Figure 9.6)
Simple fistulous tract (fistula) (Figure 9.7)	Hypoechoic or anechoic band-like dermal or hypodermal structure dermal connected to the base of widened hair follicles (Figure 9.8)
Complex fistula (fistula) (Figure 9.9)	Two or more connected fistulous tracts in the same region (non-linear fistulas) (Figure 9.10)

0 (17).png

Table 12.1 Differential diagnosis of HS

Common disorders	Less common disorders
Follicular pyoderma (folliculitis)	Inflamed or superinfected apocrine glands cyst
Furuncle	Sebaceous/trichilemmal cyst
Carbuncle	Steatocystoma multiplex
Giant comedo	Acne keloidalis nuchae
	Acne fulminans
	Rosacea fulminans
	Pilonidal cyst
	Amicrobial pustulosis of the folds
	Pyoderma gangrenosum
	Crohn's disease
	Lymphogranuloma venereum
	Syphilis

0 (18).png

Table 11.1 Diagnostic criteria of hidradenitis suppurativa (adopted by the Second International Conference on Hidradenitis suppurativa, March 5, 2009, San Francisco, CA US)

1. Typical lesions, i.e., deep-seated painful nodules: 'blind boils' in early lesions; abscesses, draining sinuses, bridged scars and 'tombstone' double-ended pseudo-comedones in secondary lesions
2. Typical topography, i.e., axillae, groins, perineal and perianal region, buttocks, infra and inter mammary folds
3. Chronicity and recurrences

All three criteria must be met for establishing the diagnosis

Milder cases may be diagnosed as simple boils but the recurrent nature and distribution of the sores should help make the diagnosis. Severe cases are more obvious with recurrent abscesses, sinuses and scars. Lesions persist for months

Table 11.2 Hurley stages for hidradenitis suppurativa

• Stage 1—solitary or multiple isolated abscesses without scarring or sinus tracks
• Stage 2—recurrent abscesses, single or multiple widely separated lesions with sinus track formation
• Stage 3—diffuse or broad involvement with multiple interconnecting sinus tracks and abscesses

Table 11.3 Differential diagnosis of hidradenitis suppurativa

Infections:
Bacterial—Carbuncles, furuncles, abscesses, ischiorectal/perirectal abscesses, Bartholin's duct abscess
Mycobacteria—TB
STI—Granuloma inguinale, lymphogranuloma venereum, syphilis
Deep fungi—Blastomyces
Tumors or cysts:
Epidermoid cysts, Bartholin's cysts, pilonidal sinus
Miscellaneous:
Crohn's disease, anal or vulvovaginal fistulae

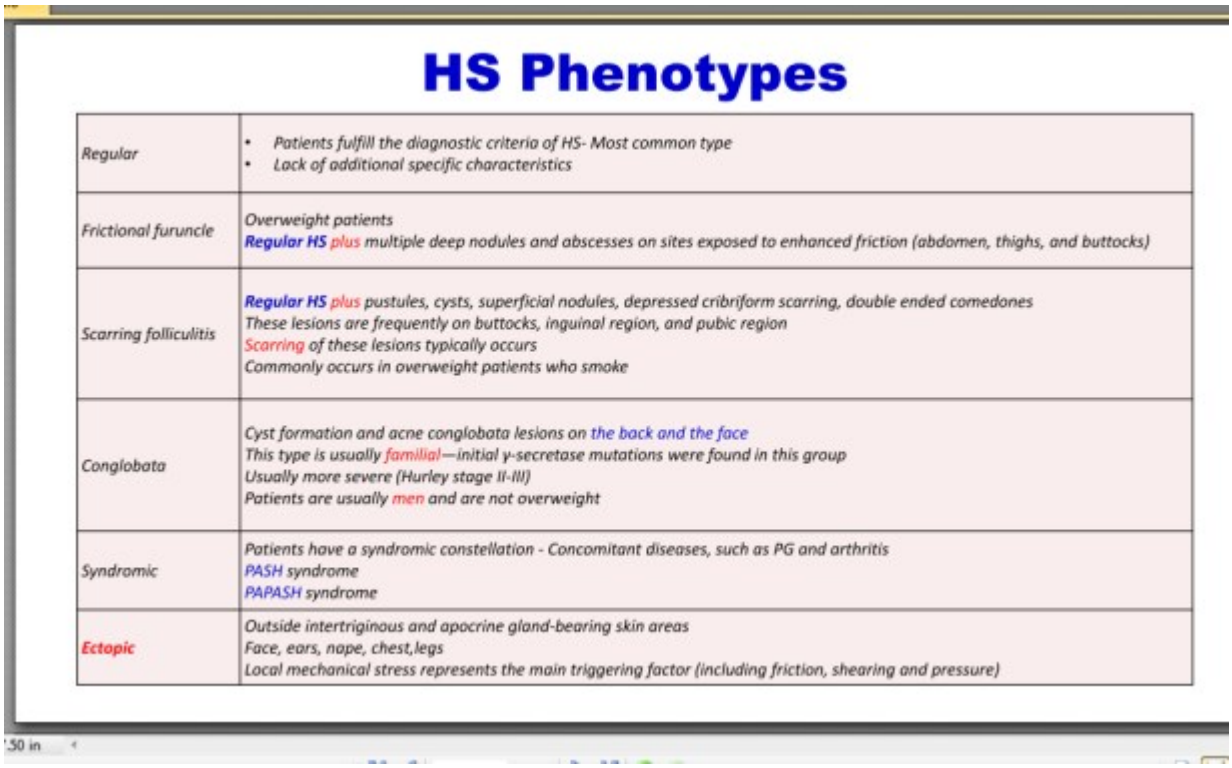
Table 36.1 Hurley stage classification for HS patients

Stage I	Abscess formation, single or multiple, without sinus tracts or scarring
Stage II	Recurrent abscesses with sinus tract formation or scarring
	Single or multiple, widely separated lesions
Stage III	Diffuse or near-diffuse involvement or multiple interconnected sinus tracts and abscesses across entire anatomic region

Modified from: Hurley H. Axillary hyperhidrosis, apocrine bromhidrosis, hidradenitis suppurativa, and familial benign pemphigus. In: Roenigk RK and Roenigk HH Jr., editors. Dermatologic Surgery: Principles and Practice. New York: Marcel Dekker; 1989. pg. 631–643

As a result, patients' improvement from their "baseline" disease activity, assessed at the time of initiation of an investi-

0 (2).PNG



HS Phenotypes

Regular	• Patients fulfill the diagnostic criteria of HS- Most common type • Lack of additional specific characteristics
Frictional furuncle	Overweight patients **Regular HS** plus multiple deep nodules and abscesses on sites exposed to enhanced friction (abdomen, thighs, and buttocks)
Scarring folliculitis	**Regular HS** plus pustules, cysts, superficial nodules, depressed cribriform scarring, double ended comedones These lesions are frequently on buttocks, inguinal region, and pubic region Scarring of these lesions typically occurs Commonly occurs in overweight patients who smoke
Conglobata	Cyst formation and acne conglobata lesions on the back and the face This type is usually familial—initial γ-secretase mutations were found in this group Usually more severe (Hurley stage II-III) Patients are usually men and are not overweight
Syndromic	Patients have a syndromic constellation - Concomitant diseases, such as PG and arthritis PASH syndrome PAPASH syndrome
Ectopic	Outside intertriginous and apocrine gland-bearing skin areas Face, ears, nape, chest,legs Local mechanical stress represents the main triggering factor (including friction, shearing and pressure)

TABLE 20-4 Treatment Based on Hurley Stage

Stage I	Stage II	Stage III
1. Topical clindamycin 1% solution 2. Antibiotics (7- to 10-d courses) • Tetracyclines • Amoxicillin-clavulanate • Clindamycin 3. Intralesional triamcinolone	1. Long-term tetracycline or dapsone for maintenance 2. Clindamycin + rifampin for 3 mo if severe inflammation and little scarring 3. Intralesional triamcinolone	1. Antibiotics 2. Corticosteroids (short-term relief for flares) and/or acitretin 3. Surgery

A. Lifestyle Modifications

0 (21).png

Table 6-5 Treatment Recommendations for HS

HURLEY STAGE	THERAPY
Primary	Topical antibiotics Clindamycin 1% solution BID Benzoyl peroxide 5%–10% solution or wash BID Chlorhexidine 4% solution BID
Secondary	Topical antibiotics + Systemic antibiotics: Doxycycline 50–100 mg BID or minocycline 50–100 mg BID Amoxicillin 250–500 mg BID Sulfamethoxazole/trimethoprim DS BID Clindamycin 300 mg BID Antiandrogen (Females PRN): Spironolactone 50–200 mg QD
Tertiary	Topical antibiotics + systemic antibiotics Other therapies: Dapsone, finasteride, isotretinoi Immunomodulators: Systemic steroids, infliximab, etanercept, cyclosporin Antiandrogen PRN
Independent of severity	Adjunctive therapy (weight loss, smoking cessation, sitz bath, warm compresses, intralesional steroids) Pain management (nonsteroidal anti-inflammatories, opiates) Surgical excision

Table 42.1 Severity classification of hidradenitis suppurativa according to Hurley staging

Stage I	Abscess formation, single or multiple, without sinus tracts and cicatrisation
Stage II	Recurrent abscesses with tract formation and cicatrisation, single or multiple, widely separated lesions
Stage III	Diffuse or near-diffuse involvement or multiple interconnected tracts and abscesses across the entire area

Diagnosis and Differential Diagnosis

- Crohn's dis
  HS has to
  case of sole
  cannot be
  HS. There
  disease.
- Acne vulgar
  edones and
  lesions.

General Prir

Management o

0 (23).png

Table 46.1 Pathogenic hypotheses in HS and associated evidence

Genetic	About one-third of patients have an affected first-degree relative. Rarely, pathogenic mutations in γ-secretase, a protein involved in keratinocyte differentiation, are present. Genetic testing is not routinely offered.
Environmental	Smoking and obesity are strong risk factors but HS can develop in non-smokers of normal BMI.
Endocrine	Suggested by onset soon after puberty, female preponderance and menstrual exacerbations in some patients.
Microbiological/immune dysregulation	Skin bacteria are present in subcutaneous HS biopsies but this may be due to non-sterile skin tunnels. Pro-inflammatory cytokines are increased in HS lesions.

0 (24).png

Table 46.2 Diagnostic criteria for HS

Typical lesions	Some of: deep-seated painful nodules, abscesses, draining skin tunnels, rope-like scars and multiheaded open pseudocomedones (see Figure 46.1)
Predominantly flexural location	Axillae, groins, perineal, natal cleft, buttocks, infra- and intermammary folds
Chronicity and recurrence	Multiple and/or recurrent lesions occurring over time

0 (25).png

Box 13.1 shows a list of relevant investigations.

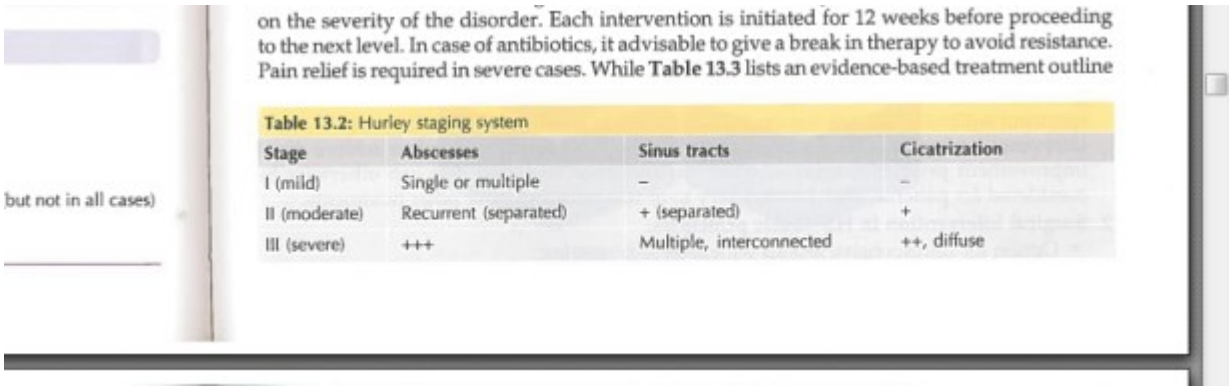
Table 13.1: Differential diagnosis of HS

Disease	Similarity	Dissimilarity
Crohn disease	Perianal and genital fistulae, abscesses, scars	'Knife-cut' ulcers; fistulae communicate with the gastrointestinal tract; often concurrent with gastrointestinal Crohn disease; no comedones
Intergluteal pilonidal disease	Sinus tract formation; swollen, inflamed, and painful lesions; can occur in patients with hidradenitis suppurativa	Localization, recurrence is limited to the intergluteal area
Furuncles and carbuncles	Painful nodules and abscesses	Lack of chronicity
Tuberculosis (lupus vulgaris)	Chronic inflammation and scarring	Absence of polyporous comedones, fistulae and sinuses
Lymphogranuloma venereum	Localization in the genital and inguinal folds	Bacterial etiology: *Chlamydia trachomatis* (serotype L1–L3)

Box 13.1: Investigations in HS

- Leukocytosis, elevated erythrocyte sedimentation rate
- Low serum iron levels

0 (26).png



but not in all cases)

on the severity of the disorder. Each intervention is initiated for 12 weeks before proceeding to the next level. In case of antibiotics, it advisable to give a break in therapy to avoid resistance. Pain relief is required in severe cases. While **Table 13.3** lists an evidence-based treatment outline

Table 13.2: Hurley staging system

Stage	Abscesses	Sinus tracts	Cicatrization
I (mild)	Single or multiple	–	–
II (moderate)	Recurrent (separated)	+ (separated)	+
III (severe)	+++	Multiple, interconnected	++, diffuse

0 (27).png

Table 13.3: Evidence-based treatment of HS

		Mild	Moderate	Severe
1st line	Medical	• Clindamycin gel (1%) • Resorcinol (15%)	• Doxycycline/ minocycline (50–100 mg) BD/lymecycline 408 mg	• Clindamycin + Rifampicin × 10 wks[1] • Adalimumab × 12 wks[3]
	Surgical	Intralesional triamcinolone (3–5 mg) one injection	Excision, carbon dioxide laser evaporation, drainage of abscesses	
2nd line	Medical		Clindamycin + Rifampicin × 10 wks[1]	Prednisone (40–60 mg) daily for 3–4 days then taper OR Cyclosporine (3–5 mg/kg) daily
	Surgical		Local procedures for sinus tracts[2]	
3rd line	Medical		• Adalimumab × 12 wks[3] • Dapsone (25–200 mg) daily • Acitretin (0.5 mg/kg) daily	—
	Surgical		—	• Wide excision for larger affected areas • Radical wide excision

[1]Clindamycin (300 mg) BD + Rifampicin (300 mg) BD daily. [2]Deroofing of sinus tracts, sinus tract excision, STEEP surgery, carbon dioxide laser evaporation of diseased tissue. [3]Loading doses at week 0 (160 mg SC), week 2 (80 mg SC), Maintenance (40 mg SC) weekly.

for HS, salient agents are detailed below. Here it must be noted that the cardinal feature of HS is the presence of "tunnelled comedones" which can only be cured by surgery. The other

0 (28).png

Table 4 Stage appropriate therapy of acne inversa/dissecting terminal hair folliculitis

Hurley stages	Therapy
Stage 1	Clindamycin (2–3 times 300 mg/day) (possibly clindamycin 2–3 times 300 mg/day i.v. in the first 5 days) (or minocyclin 100 mg/day orally) in combination with rifampicin 2 times 300 mg/day orally over 1–3 months
Stage 2	As stage 1, limited excision of locally recurrent lesions
Stage 3	As stage 1, infliximab (5.0 mg/kg body weight i.v.) or adalimumab (40 mg s.c.) once or twice
	Radical excision of the affected area with 1–2 cm safety margin
General information	Abstinence from smoking, weight reduction
	Local disinfectant measures
	In women with signs of hyperandrogenism/hyperandrogenemia endocrinological clarification and use of antiandrogens (in particular antiandrogenic contraceptives with cyproterone acetate)

in hairdressers. Often there is a symptom-free opening on the

0 (29).png

Box 90.1 Essential criteria for a diagnosis of hidradenitis suppurativa to be made

1 Typical lesions	Deep-seated painful nodules, abscesses, draining tunnels, bridged scars and paired or multiheaded open pseudocomedones
2 Typical topography	Axillae, groin, perineal and perianal region, buttocks, infra- and intermammary folds
3 Chronicity and recurrence of lesions	Recurrent flares of painful lesions over time in the same or differing skin sites (at least two flares in a 6-month period)

0 (3).png

Table 5.1 Diseases with an association with HS

Crohn's disease
Irritable bowel syndrome
Down's syndrome
Arthritis
Graves' disease
Hashimoto thyroiditis
Sjogren's syndrome
Hyperandrogenism
Herpes simplex
Acanthosis nigricans

Table 5.2 Apocrine gland areas of the body prone to HS

Axillae
Inguinal folds
Inframammary areas
Perineal areas
Buttocks
Scrotum
Mons pubis
Abdominal folds

0 (30).png

Table 90.1 Definition of the three Hurley stages in hidradenitis suppurativa.

Stage	Features
I (Figure 90.13)	Recurrent inflammatory skin lesions without skin tunnels and scarring
II (Figure 90.14)	Recurrent inflammatory skin lesions with widely separated skin tunnels and scarring
III (Figure 90.15)	Multiple interconnected inflammatory lesions, skin tunnels and scarring diffusely involving an entire skin region

0 (31).png

Table 111.2 Hurley severity stages.

Stage	Definition
Stage I	Solitary or multiple abscesses occurring without formation of sinus tracks or scarring
Stage II	Recurrent abscesses with sinus track formation and scarring occurring within an anatomical region but separated by areas of normal skin
Stage III	Confluent involvement of an entire anatomical region with multiple interconnected abscesses, nodules, sinus tracks and scarring

Adapted from [5].

tration of
: without
activation
upport to
essarily a
nd in all
hough its
($P = 0.04$)
in LCH,
d because
nutations.

Table 135.1 Distribution of Langerhans cell histiocytosis in 170 children with single system-Langerhans cell histiocytosis treated in the DAL-HX studies.

Sites	Patients (%)
Unifocal bone	68
Multifocal bone	19
Isolated skin	11
Isolated lymph node	2

Reproduced from Titgemeyer *et al*. 2001 [23] with permission of John Wiley & Sons.

0 (33).png

Box 83-4

Differential Diagnosis of Hidradenitis Suppurativa

- Abscesses (including from methicillin-resistant *Staphylococcus aureus*)
- Furuncles/carbuncles
- Actinomycosis
- Cat scratch disease
- Donovanosis
- Lymphogranuloma venereum
- Lymphadenitis
- Infected Bartholin cyst
- Crohn disease
- Ulcerative colitis
- Tuberculosis
- Tularemia
- Ruptured epidermal cyst

From Jovanovic M et al: Hidradenitis suppurativa, in *emedicine*, edited by Siegel D et al. (http://www.emedicine.com), 2006.

Clinical Findings

0 (34).png

in
-1
lso
ith
of
ith
ıce
ore
ith
HS
or-
of

TABLE 84-1
Diagnostic Criteria

1. **Typical lesion (1 or more):** painful nodules, abscesses, draining sinuses, double-open comedones, bridged scars
2. **Typical distribution[a]:** axillae, groin, buttocks, perineal, and infra-mammary regions
3. **Chronicity and recurrence** of symptoms

[a]Atypical or ectopic sites may be affected but at least 1 typical area must be involved.

systems, however, are generally considered too cumbersome for clinical practice but remain useful in research settings.

TABLE 84-2
Differential Diagnosis for Hidradenitis Suppurativa

EARLY LESIONS	LATE LESIONS
Acne vulgaris	Actinomycosis
Carbuncle	Anal fistula
Cellulitis	Cat scratch disease
Cutaneous blastomycosis	Crohn disease
Dermoid cyst	Granuloma inguinale
Erysipelas	Ischiorectal abscess
Folliculitis	Lymphogranuloma venereum
Furuncle	*Nocardia* infection
Inflamed epidermoid cysts	Noduloulcerative syphilis
Lymphadenopathy	Pilonidal disease
Perirectal abscess	Tuberculosis abscess
Pilonidal cyst	Tularemia

Adapted from Alikhan A, Lynch PJ, Eisen DB. Hidradenitis suppurativa: a comprehensive review. *J Am Acad Dermatol.* 2009;60(4):539-61.

considered: I&D, incision and drainage. (From Alikhan A, Lynch PJ, Eisen review. *J Am Acad Dermatol*. 2009;60[4]:539-561, with permission. Copyri

TABLE 84-3
Hurley Staging

HURLEY STAGE	CHARACTERISTICS
I	Recurrent abscesses without scarring or sinus tract formation
II	Recurrent abscesses with scarring and sinus tract formation separated by normal skin
III	Recurrent abscesses, diffuse scarring, and interconnecting sinus tracts with minimal to no normal skin between lesions

HIST

Follicula
histopath
ease dur
follicular
licles, hy
perifollic
plugging
histologi
and rup

0 (37).png

Table I. Treatments for HS: Approved or seeking FDA approval

	Adalimumab (TNF inhibition)	Secukinumab (IL-17 A inhibitor) and Bimekizumab (IL-17 A/F inhibitor)
Primary endpoint timeline for trials	12 wks	16 wks
Contraindications	Absolute: - Congestive heart failure - Demyelinating disorders Relative: - Malignancy in past 5 yrs - SLE	Relative: - IBD (some pts with well-controlled IBD were included in trials) - Recurrent oropharyngeal candidiasis
Approved comorbidities	RA; Uveitis; IBD AS; PSA/PSO	AS PSA/PSO
Side effects	Immunosuppression Infection Paradoxical rashes Rare new-onset MS/demyelination	Mucocutaneous candidiasis (thrush primarily) Paradoxical rashes New onset IBD (rare)
Pediatric considerations	Approved for children >12 yo for HS	Not approved for children for HS.
Drug survival	Higher rates of anti-drug antibody development	Lower rates of anti-drug antibody development

AS, Ankylosing spondylitis; *FDA*, Food and Drug Administration; *HS*, hidradenitis suppurativa; *IBD*, inflammatory bowel disease; *PSA*, psoriatic arthritis; *PSO*, psoriasis; *RA*, rheumatoid arthritis; *SLE*, systemic lupus erythematosus; yo, years old.

0 (38).png

to be determined, minimizing mechanical stress may be an important aspect of managing HS symptoms.

potentially offer new avenues for targeted therapies for HS.[55]

Table I. Extrinsic factors associated with hidradenitis suppurativa and their suspected mechanism

Extrinsic factors	Suspected mechanism
Environment	
Friction	Causes micro-injury of the skin, which leads to release of damage-associated molecular patterns.
Shear forces	
Pressure	
Warm weather	Sweating in association with increased heat may increase friction and hyperkeratosis.
Skin and gut microbiome	Dysbiosis in the skin and gut microbiota induces inflammation and immune dysregulation.
Lifestyle	
Tobacco use	Nicotine stimulates chemotaxis, cytokine release, and oxidative stress and promotes keratinocyte differentiation and epithelial hyperplasia. Carbon monoxide and hydrogen cyanide found in tobacco smoke hinder the wound healing of lesions.
Excess body weight	Larger skin surface in the skin folds increases friction and moisture.
Diet	Intake of dairy, high-fat foods, and high-glycemic diets may promote systemic inflammation, insulin resistance, and increased androgen levels.
Medication	
Adalimumab	Inhibiting subsets of cytokines induces an imbalance favoring another immune response pattern.
Infliximab	
Etanercept	
Secukinumab	
Ixekizumab	
Ustekinumab	
Canakinumab	

0 (39).png

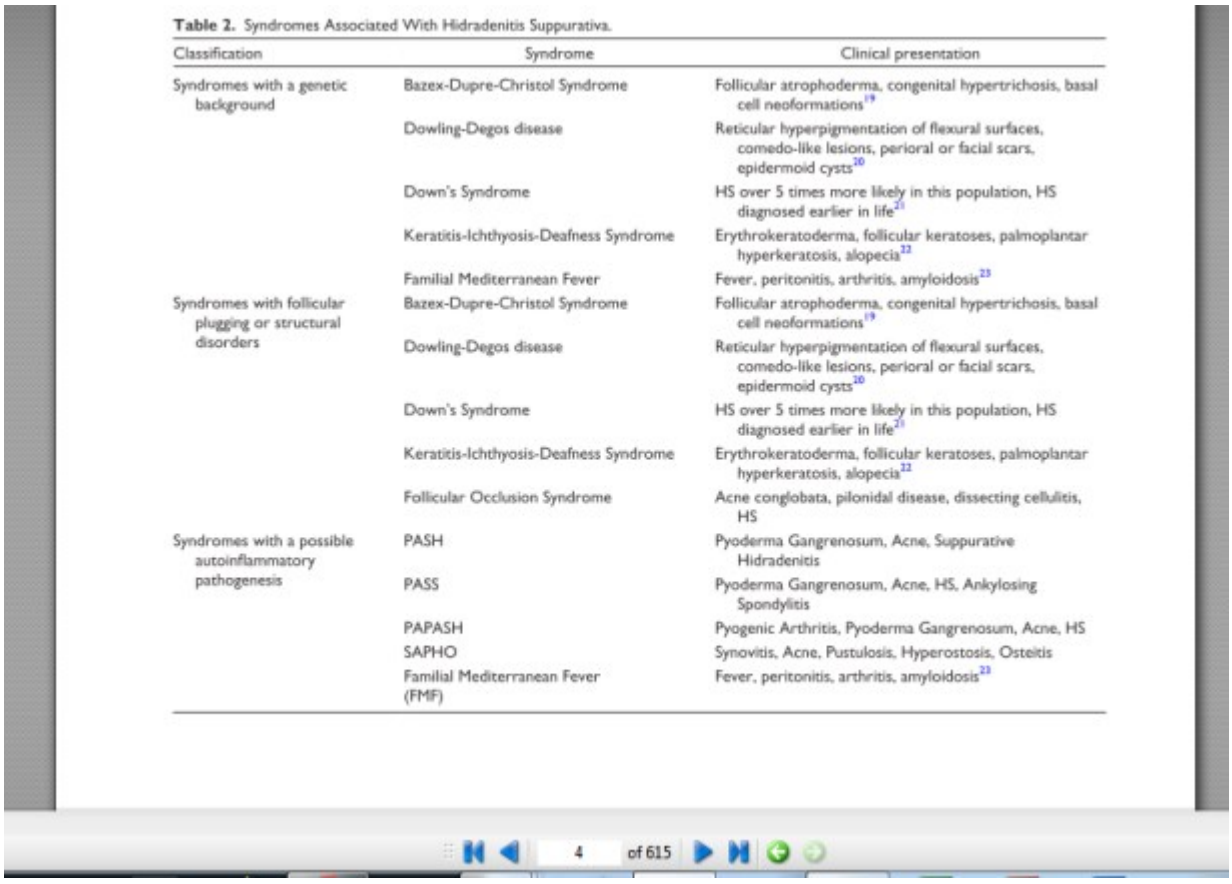


Table 2. Syndromes Associated With Hidradenitis Suppurativa.

Classification	Syndrome	Clinical presentation
Syndromes with a genetic background	Bazex-Dupre-Christol Syndrome	Follicular atrophoderma, congenital hypertrichosis, basal cell neoformations[19]
	Dowling-Degos disease	Reticular hyperpigmentation of flexural surfaces, comedo-like lesions, perioral or facial scars, epidermoid cysts[20]
	Down's Syndrome	HS over 5 times more likely in this population, HS diagnosed earlier in life[21]
	Keratitis-Ichthyosis-Deafness Syndrome	Erythrokeratoderma, follicular keratoses, palmoplantar hyperkeratosis, alopecia[22]
	Familial Mediterranean Fever	Fever, peritonitis, arthritis, amyloidosis[23]
Syndromes with follicular plugging or structural disorders	Bazex-Dupre-Christol Syndrome	Follicular atrophoderma, congenital hypertrichosis, basal cell neoformations[19]
	Dowling-Degos disease	Reticular hyperpigmentation of flexural surfaces, comedo-like lesions, perioral or facial scars, epidermoid cysts[20]
	Down's Syndrome	HS over 5 times more likely in this population, HS diagnosed earlier in life[21]
	Keratitis-Ichthyosis-Deafness Syndrome	Erythrokeratoderma, follicular keratoses, palmoplantar hyperkeratosis, alopecia[22]
	Follicular Occlusion Syndrome	Acne conglobata, pilonidal disease, dissecting cellulitis, HS
Syndromes with a possible autoinflammatory pathogenesis	PASH	Pyoderma Gangrenosum, Acne, Suppurative Hidradenitis
	PASS	Pyoderma Gangrenosum, Acne, HS, Ankylosing Spondylitis
	PAPASH	Pyogenic Arthritis, Pyoderma Gangrenosum, Acne, HS
	SAPHO	Synovitis, Acne, Pustulosis, Hyperostosis, Osteitis
	Familial Mediterranean Fever (FMF)	Fever, peritonitis, arthritis, amyloidosis[23]

0 (4).png

Table 3.1 Lesion type and definition

Type	Clinical definition	Ultrasound definition
Nodule (pseudocyst)	Raised lesion, round, diameter >10 mm, three-dimensional	Round- or oval-shaped hypoechoic or anechoic nodular dermal and/or hypodermal structure
Abscess (fluid collection)	Swelling lesion, three-dimensional containing fluid (pus)	Hypoechoic or anechoic fluid dermal and/or hypodermal deposits connected to the base of widened hair follicles
Fistulous tract (tunnel)	Opening of variable length and depth, ending at the skin surface, and sometimes oozing a fluid	Hypoechoic or anechoic band-like dermal or hypodermal structure dermal connected to the base of widened hair follicles
Complex fistula (multitunnel)	The presence of numerous tunnels in a localized skin area; almost always, these tunnels may be interconnected	Two or more connected fistulous tracts in the same region

Wortsman et al. [51] and Lipsker et al. [53] modified

0 (40).png

Table 2 - Hurley staging*.

Stage I - Abscess formation, single or multiple, without sinus tracts and cicatrization
Stage II - Recurrent abscesses with tract formation and cicatrization, single or multiple, widely separated lesions
Stage III - Diffuse or near-diffuse involvement or multiple interconnected tracts and abscesses across the entire area.

*Adapted from Hurley.[6]

therapeutic efficacy.[1,4] Fig.s 1, 2 and 3 illustrate typical cases of HS patients with Hurley 1 to 3 disease, respectively. Recently, a revised version of Hurley staging was proposed.[6]

Figu

0 (41).png

Several infectious and non-infectious dermatoses need to be differentiated from HS (Table 1).

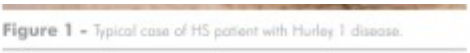


Figure 1 - Typical case of HS patient with Hurley 1 disease.

Table 1 - Differential diagnosis of hidradenitis suppurativa*.

Carbuncle	Cutaneous Crohn disease	Nodulaulcerative syphilis
Epidermoid/dermoid cyst	Simple abscesses	Blastomycosis
Erysipelas	Neoplasms	Scrofuloderma (Tuberculosis)
Furuncle	Lymphogranuloma venereum	Granuloma Inguinale/Donovanosis
Pilonidal cyst	Cutaneous actinomycosis	

*Adapted from Zouboulis et al.[1]

0 (42).png

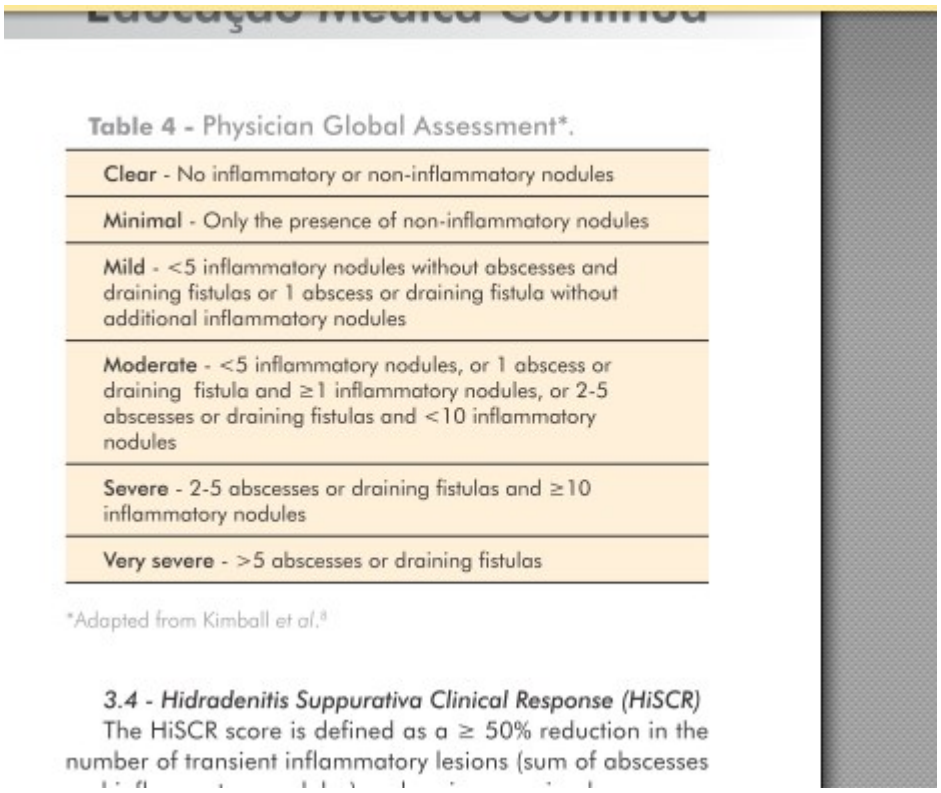


Table 4 - Physician Global Assessment*.

Clear - No inflammatory or non-inflammatory nodules
Minimal - Only the presence of non-inflammatory nodules
Mild - <5 inflammatory nodules without abscesses and draining fistulas or 1 abscess or draining fistula without additional inflammatory nodules
Moderate - <5 inflammatory nodules, or 1 abscess or draining fistula and ≥1 inflammatory nodules, or 2-5 abscesses or draining fistulas and <10 inflammatory nodules
Severe - 2-5 abscesses or draining fistulas and ≥10 inflammatory nodules
Very severe - >5 abscesses or draining fistulas

*Adapted from Kimball *et al.*[8]

3.4 - Hidradenitis Suppurativa Clinical Response (HiSCR)

The HiSCR score is defined as a ≥ 50% reduction in the number of transient inflammatory lesions (sum of abscesses

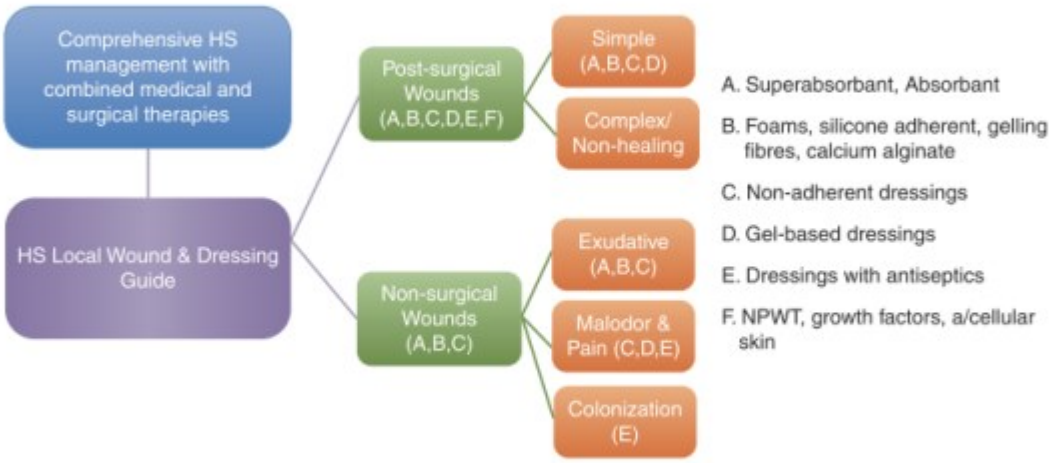

Comprehensive HS management with combined medical and surgical therapies
HS Local Wound & Dressing Guide
Post-surgical Wounds (A,B,C,D,E,F)
Non-surgical Wounds (A,B,C)
Simple (A,B,C,D)
Complex/ Non-healing
Exudative (A,B,C)
Malodor & Pain (C,D,E)
Colonization (E)
A. Superabsorbant, Absorbant
B. Foams, silicone adherent, gelling fibres, calcium alginate
C. Non-adherent dressings
D. Gel-based dressings
E. Dressings with antiseptics
F. NPWT, growth factors, a/cellular skin

Fig. 18.3 Algorithm for providing optimal wound dressings in hidradenitis suppurativa. (Modified from Alavi, Sibbald, & Kirsner, J Dermatol Treatment, 2017 [17])

nology. Absorbent dressings, on the other hand,

films in tissue samples from a patient with HS [6].

Table 18.1 Hurley stages 1–3

Stage 1: Single or multiple abscesses with no scarring or sinus tracts
Stage 2: Recurrent abscesses with sinus tract formation
Stage 3: Diffuse involvement with interconnected sinus tracts and multiple abscesses

matologists, Updates in Clinical

0 (5).png

Table 3.3 HS-PGA scale

Stage	Description
Clear	No inflammatory or non-inflammatory nodules
Minimal	Only the presence of non-inflammatory nodules
Mild	Fewer than five inflammatory nodules or one abscess or draining fistula and no inflammatory nodules
Moderate	Fewer than 5 inflammatory nodules or 1 abscess or draining fistula and 1 or more inflammatory nodules or 2–5 abscesses or draining fistulas and fewer than 10 inflammatory nodules
Severe	Two to 5 abscesses or draining fistulas and 10 or more inflammatory nodules
Very severe	More than five abscesses or draining fistulas

Kimball et al. modified [62]

- Stage III: Five or more fluid collections or two

0 (6).png

Table 3.2 Clinical staging and severity scales

Score
• Hurley staging system
• Modified Sartorius Score (MSS)
• HS-Physician's Global Assessment (HS-PGA)
• Acne Inversa Severity Index (AISI)
• Hidradenitis Suppurativa Severity Index (HSSI)
• Hidradenitis Suppurativa Severity Score System (IHS4)
• Hidradenitis Suppurativa Clinical Response (HiSCR)

Table 20.8 Differential diagnosis of hidradenitis suppurativa

Condition	Differentiating factors
Acne vulgaris	Primarily on face, chest, back No sinus tracts or extensive scarring
Folliculitis, carbuncles, furuncles	Transient lesions Usually respond to appropriate antibiotics No comedones, sinus tracts, hypertrophic scars
Pilonidal cyst	Isolated to area of the natal cleft May occur in conjunction with HS
Granuloma inguinale	Enlarging ulcer with an undermined border Visualization of Donovan bodies
Perianal Crohn's disease	History of gastrointerstinal Crohn's disease Classic "knife-cut" ulcers Rectovaginal and rectoperineal fistulas

0 (8).png

Table 20.9 Patient education, support, and lifestyle modifications in the management of hidradenitis suppurativa

- Patient education and support [125]
  - Inquire about impact on quality of life and symptoms of depression
  - Provide psychological support or refer to qualified provider
- Avoid trauma to affected areas [125]
  - Wear loose-fitting clothing
  - Do not manipulate the lesions
  - Use perfume- and dye-free laundry detergent for clothing
- Gently clean and dress the lesions daily
  - Use gentle, soap-free cleansers
  - Avoid scrubbing the area
  - Cover draining lesions and post-surgical wounds with white petrolatum, absorbent dressing, and tubular net or mesh dressings
- Other Lifestyle modification
  - Smoking cessation [126, 127]
  - Weight loss [127]
  - Low glycemic and low dairy diet [127, 128]

the antibiotic. Topical resorcinol 15%, a chemical peeling agent, has been shown to reduce pain, improve healing, and promote resolution of abscesses when applied to acutely inflamed lesions once to twice daily [132]. Intralesional corticosteroids are

0 (9).png

Table 9.4 Sonographic Scoring of Hidradenitis Suppurativa (SOS-HS)

Stage	Sonographic signs
Stage I	Single fluid collection and/or dermal changes affecting a single body segment (either one side or bilateral), without fistulous tracts
Stage II	Two to four fluid collections and/or a single fistulous tract with dermal changes, affecting up to two body segments (either one side or bilateral)
Stage III	Five or more fluid collections and/or two or more fistulous tracts with dermal changes, and/or involvement of three or more body segments (either one side or bilateral)

Adapted from Wortsman et al. [57]; with permission of Dermatologic Surgery

Table 9.5 Grading of fibrosis and edema of fistulous tracts in hidradenitis suppurativa

Grade	Sonographic signs
Grading of fibrosis	
0	Absent
1	Thin peripheral hypoechoic band (intermittent or continuous) with a fibrillar pattern
2	Thick and continuous peripheral hypoechoic band with a fibrillar pattern that invades the lumen of the tract and produces a hypoechoic "halo" sign in transverse view (intermittent or continuous)
Grading of edema	
0	Absent
1	Diffuse increase of the echogenicity of the hypodermis
2	Prominent hyperechoic hypodermal fatty lobules, with anechoic fluid between the fatty lobules

Adapted from Wortsman et al. [62]; with permission from Elsevier

HIDRADENITIS SUPPURATIVA – GRADING SYSTEMS AND THERAPEUTIC LADDER	
Hurley staging system	
Stage I – one or more abscesses with no sinus tract or scar formation Stage II – one or more widely separated recurrent abscesses, with sinus tract and scar formation Stage III – multiple interconnected sinus tracts and abscesses throughout an affected region; more extensive scarring	
Sartorius grading system[79]	
• Anatomical regions involved: axilla (left +/or right), groin (left +/or right), gluteal (left +/or right) or other region (e.g. inframammary): 3 points per region involved • Number and scores of lesions for each region: nodules = 1; fistulae = 6 • The longest distance between two relevant lesions*, i.e. nodules and fistulae, in each region: <5 cm = 1; 5–10 cm = 3; >10 cm = 9 • Are all lesions clearly separated by normal skin? In each region – yes 0/no (Hurley III) 9	
Therapeutic ladder	
Indication	*Therapeutic interventions*
General measures	• If obese or overweight, weight reduction • Reduce friction and moisture via loose undergarments, absorbent powders, and topical aluminum chloride • Antiseptic soaps • Smoking cessation
Hurley Stage I	• Intralesional triamcinolone (5 mg/ml) injections into early inflammatory lesions • Topical clindamycin • Eradication of *S. aureus* carriage with topical mupirocin in nose, axillae, umbilicus, and perianal regions • Oral antibiotics tailored to results of bacterial cultures from pustular discharge or abscess contents • Oral antibiotic therapy (alone or in combination) for its anti-inflammatory effect (rifampin + clindamycin[80], tetracycline, doxycycline, minocycline, dapsone, trimethoprim–sulfamethoxazole) • Oral anti-androgen therapy (e.g. finasteride)
Hurley Stage II (see Fig. 38.15A)	• Oral antibiotic therapy (see Stage I) • Acitretin[81] • Systemic immunosuppressive agents including adalimumab[82,^], infliximab[52], and cyclosporine[83] Surgical treatments† • Limited local excisions with second intention healing • CO_2 laser ablation with second intention healing • Nd:YAG laser treatments, at least 3–4 monthly sessions
Hurley Stage III (see Fig. 38.15B)	Medical treatments outlined for Stages I and II Surgical treatments† • Early wide surgical excision of involved areas • CO_2 laser ablation with second intention healing
*Or size if only one lesion. ^FDA-approved dosing regimen: 160 mg (four 40 mg injections) on Day 1 -*or*- 80 mg daily on Days 1 and 2 followed by 80 mg on Day 15 then 40 mg on Day 29 and weekly thereafter. †Incision and drainage is discouraged given high rate of recurrence.	

Table 38.7 Hidradenitis suppurativa – grading systems and therapeutic ladder. Additional scoring systems are used in clinical trials[84]. In the Revuz modification of the Sartorius grading system, five regions (axilla, breast, inguino-femoral, perianal, perineal) are scored, with additional modifications including the addition of abscesses to fistulae. Both Hidradenitis Suppurativa Clinical Response (HiSCR) and a Physician's Global Assessment Scale have been utilized as has a refinement of the Hurley staging system in which stages I and II are subdivided into A,B,C subtypes.

TRICHOSTASIS SPINULOSA

Trichostasis spinulosa is a common, but often underdiagnosed, follicular disorder of unknown etiology. Asymptomatic comedo-like lesions that contain keratin and multiple vellus hairs are seen, primarily on the face, especially its mid to lower central portion (see Table 36.2), as well as the trunk, most often the interscapular region. Histologically, there is follicular hyperkeratosis and multiple vellus hairs enveloped by a keratotic sheath within a dilated hair follicle. Patients seek treatment because of the cosmetic appearance, but options are limited; the latter include keratolytics, depilatories, topical tretinoin and lasers (e.g. long-pulsed alexandrite, short-pulsed alexandrite, pulsed diode)[70]. There is a case report of benefit from periodic application of a hydroactive adhesive pad (Bioré®) with a recommendation for shorter exposure times in individuals with more darkly pigmented skin so as to reduce the risk of hyperpigmentation[71].

VIRAL-ASSOCIATED TRICHODYSPLASIA

Synonyms: ■ Viral-associated trichodysplasia spinulosa ■ Viral-associated trichodysplasia of immunosuppression ■ Trichodysplasia spinulosa ■ Cyclosporine-induced follicular dystrophy

Viral-associated trichodysplasia was first described in 1995 in the context of drug-induced immunosuppression in organ transplant recipients, hence its original association with cyclosporine[72]. The underlying cause is the trichodysplasia spinulosa-associated polyomavirus[73]. Skin-colored to pink follicular papules and follicular spines favor the central face (see Fig. 130.8) and they may be accompanied by loss of the eyebrows and eyelashes; extrafacial lesions with associated alopecia may also develop. Histologically, enlarged and distended anagen-type follicles have a high number of inner root sheath cells with excessive amounts of trichohyaline granules. The spicules can be identified by surface microscopy or light microscopy (spicule pull-test)[74]. If immunosuppressive therapy cannot be reduced, topical cidofovir or tazarotene gel or oral valganciclovir (900 mg once or twice daily) may be tried.

Acknowledgment

The authors would like to acknowledge the late A. Paul Kelly, MD, for his contribution to the previous editions of this chapter.

For a table on therapeutic options for acne keloidalis plus additional online figures visit www.expertconsult.com

0.pdf

Table 1. Summary of biologic drugs used in the treatment of hidradenitis suppurativa

Target	Drug	Approved by FDA in HS	Other diseases	Dosage	Pregnancy	References
TNF-α	Adalimumab	+	• Rheumatoid arthritis • Juvenile idiopathic arthritis psoriatic arthritis • Ankylosing spondylitis • Crohn's disease • Plaque psoriasis • Ulcerative colitis • Hidradenitis suppurativa (HS) • Uveitis	160 mg *s.c.* at week 0, 80 mg *s.c.* at week 2, 40 mg *s.c.* at week 4 and 40 mg *s.c.* every week or 2 weeks	–	[10]
TNF-α	Infliximab	–	• Inflammatory bowel disease (IBD) • Rheumatoid arthritis • Ankylosing spondylitis • Psoriatic arthritis • Plaque psoriasis	5–10 mg *i.v.* every 4 or 8 weeks	–	[7]
TNF-α	Certolizumab	–	• Crohn's disease • Rheumatoid arthritis • Psoriatic arthritis • Ankylosing spondylitis • Plaque psoriasis	200–400 mg *s.c.* every 2 weeks	+	[7, 19]
TNF-α	Golimumab	–	• Rheumatoid arthritis • Psoriatic arthritis • Ankylosing spondylitis • Ulcerative colitis	200 mg *s.c.* at week 0, 100 mg *s.c.* every 4 weeks or 200 mg at week 0, 2 and every 4 weeks	–	[7, 23]
TNF-α	Etanercept	–	• Rheumatoid arthritis • Plaque psoriasis • Psoriatic arthritis • Juvenile idiopathic arthritis • Ankylosing spondylitis	50 mg *s.c.* every 2 weeks	–	[9]
IL-17	Secukinumab	+	• Hidradenitis suppurativa • Plaque psoriasis • Psoriatic arthritis • Ankylosing spondylitis • Axial spondyloarthritis • Juvenile idiopathic arthritis	300 mg *s.c.* every 2 or 4 weeks	–	[7, 36]
IL-17	Bimekizumab	–	• Plaque psoriasis • Psoriatic arthritis • Axial spondyloarthritis	320 mg *s.c.* every 2 or 4 weeks	–	[40, 50]
IL-17	Brodalumab	–	Plaque psoriasis	210 mg *s.c.* every week	–	[7, 44]
IL-17	CJM112	–	–	300 mg *s.c.* for the first 5 weeks and then every 2 weeks	–	[50]
IL-17	Isokibep	–	–	160 mg *s.c.* every week	–	[50]
IL-17	Sonelokimab	–	–	120 mg and 240 mg *s.c.*	–	[50]
IL-23	Guselkumab	–	Plaque psoriasis	100 mg *s.c.* at week 0 and 4 and every 8 weeks	–	[7, 54]
IL-23	Tildrakizumab	–	Plaque psoriasis	100 mg *s.c.* at week 0 and 4 and then 200 mg every 4 weeks	–	[57]
IL-23	Risankizumab	–	• Psoriatic arthritis • Psoriasis	150 mg *s.c.* at week 0 and 4 and every 12 weeks	–	[7]
IL-23/ /IL-12	Ustekinumab	–	• Psoriatic arthritis • Plaque psoriasis • Crohn's disease	45 mg *s.c.* or 90 mg *s.c.* if weight > 100 kg at week 0, 4, 16, 28	–	[10]
IL-1	Anakinra	–	• Rheumatoid arthritis • Cryopyrin-associated periodic syndromes • Interleukin-1 receptor antagonist deficiency	100 mg s.c. or 200 mg daily	–	[9, 10, 69]
IL-1	Canakinumab	–	Periodic fever syndromes, active Still's disease, gout flares	Every week/4 weeks/8 weeks — 150 mg *s.c.*	–	[7,74,75]
IL-1	Bermekimab	–	–	7.5 mg/kg every 14 days up to 7 infusions	–	[7,10]

IL — Interleukin; HS — hidradenitis suppurativa; IBD — inflammatory bowel disease; *s.c.* — subcutaneous

0.pdf

TABLE 20-1 Hurley Stages

Stage I	Abscess formation, single or multiple without sinus tracts and scar
Stage II	Recurrent abscesses with tract formation and scar formation, single or multiple widely separated lesions
Stage III	Diffuse or near-diffuse involvement, or multiple interconnecting tracts and abscesses across entire area

TABLE 20-2 Diseases Associated with Hidradenitis Suppurativa

Follicular tetrad—follicular occlusive disease

- Acne vulgaris/conglobata
- Dissecting cellulitis
- Pilonidal cysts/sinuses

Rheumatologic diseases

- Arthritis
- Synovitis, acne, pustulosis, hyperostosis, and osteitis (SAPHO) syndrome

Miscellaneous

- Crohn disease
- Pyoderma gangrenosum
- Dowling-Degos and Kitamura disease

TABLE 20-3 Differential Diagnosis of Hidradenitis Suppurativa

Infections	• Carbuncles, furuncles, and abscesses (including tuberculous) • Deep fungal infection • Sexually transmitted infections (granuloma inguinale, lymphogranuloma venereum, and noduloulcerative syphilis)
Tumors	• Cysts (epidermoid, Bartholin, and pilonidal)
Other	• Crohn disease • Anal or vulvovaginal fistulae

IV. TREATMENT

HS is very difficult to treat, and there is often only partial response to therapy. Few randomized, controlled trials exist regarding HS treatments. Consequently, most treatment options are based upon case reports or case series. One strategy is to select the treatment appropriate for the severity based on Hurley stages (Table 20-4).

(c) 2015 Wolters Kluwer. All Rights Reserved.

0.pdf

	Calculation	Total points
Anatomical region involved: armpit, breast, inguinofemoral, perianal, perineal	(# of individual sites involved x 3)	= ____
Types of lesions	# of fistulas x 4	= ____
	# of nodules x 2	= ____
	# of abscesses x 1	= ____
	# of scars x 1	= ____
	# of other (folliculitis, pustules) x 0.5	= ____
Total area involved by lesions • Record longest distance between two lesions in each affected region OR • record the size of the lesion if only one lesion present in a region	(# of regions with <5 cm distance between 2 lesions) x 2	= ____
	(# of regions with 5–10 cm distance between 2 lesions) x 4	= ____
	(# of regions with >10 cm distance between 2 lesions) x 8	= ____
Are all lesions clearly separated by normal skin?	Yes = 0	= ____
	No = 6	= ____
Total Score		= ____

Table 4.2 Modified Hidradenitis Suppurativa Score.

Rating	Description
Clear	Zero abscesses, draining fistulas, inflammatory nodules, and non-inflammatory nodules
Minimal	Zero abscesses, draining fistulas, inflammatory nodules, and non-inflammatory nodules
Mild	Zero abscesses and draining fistulas
	1–4 inflammatory nodules
	OR
	1 abscess or draining fistula and 0 inflammatory nodules
Moderate	Zero abscesses, draining fistulas, and ≥5 inflammatory nodules
	OR
	1 abscess or draining fistula and ≥1 inflammatory nodule
	OR
	2-5 abscesses or draining fistulas and <10 inflammatory nodules
Severe	2-5 abscesses or draining fistulas and ≥10 inflammatory nodules
Very severe	>5 abscesses or draining fistulas

Table 4.3 Hidradenitis Physician Global Assessment Scale.

0.pdf

Table 52.1: Treatment approaches for diseases of the follicular occlusion tetrad.

	Hidradenitis suppurativa	*Acne conglobata*	*Pilonidal cyst*	*Dissecting cellulitis of the scalp*
Steroids (systemic, intralesional)	Intralesional beneficial during acute flares	Intralesional beneficial during acute flares	Unlikely to be beneficial	Intralesional beneficial during acute flares
Antibiotics (oral, IV, topical)	Beneficial during acute flares	Beneficial during acute flares	May be beneficial during acute flares and postoperatively	Beneficial during acute flares
Non-steroidal anti-inflammatory agents (systemic, topical)	Dapsone has been suggested as an alternative therapy	Dapsone has been suggested as an alternative therapy	Not assessed	Dapsone has been suggested as an alternative therapy
Isotretinoin	May be somewhat beneficial	First-line therapy for qualified patients	Surgical intervention is key to treatment	Considered first-line therapy for moderate to severe disease
TNFα inhibitors	FDA-approved indication for adalimumab only (June 2016); infliximab also beneficial in studies	Efficacious off-label for refractory disease	Not assessed	Efficacious off-label for refractory disease
IL-1 inhibitors	Efficacious off-label for refractory disease	Efficacious off-label for refractory disease	Not assessed	Efficacious off-label for refractory disease
IL-17 inhibitors	Efficacious off-label for refractory disease	Efficacious off-label for refractory disease	Not assessed	Efficacious off-label for refractory disease
Surgical intervention	Indicated for many patient with extensive disease after acute inflammatory phase is treated	Not assessed	Indicated for all patients once acute inflammatory phase is treated	Not assessed
Laser treatment	Efficacious off-label for refractory disease	Efficacious off-label for refractory disease	Not indicated	Efficacious off-label for refractory disease

occluding clothing. An antibiotic cleanser such as benzoyl peroxide or chlorhexidine may be beneficial in reducing microbial-triggered flares. During active flares, antibiotics are often a first-line therapy, including topical clindamycin or erythromycin and systemic antibiotics such as doxycycline or clindamycin. For moderate to severe flares, there is evidence for the benefit of rifampin and dapsone, though neither has been studied in a controlled clinical trial setting. Intralesional corticosteroid therapy is another option to treat localized lesions. For severe, treatment-resistant disease, adalimumab (Humira), a subcutaneously injected TNFα inhibitor, is FDA approved. Interestingly, a comparison of the outcomes achieved with IV-administered infliximab versus adalimumab suggest that infliximab is more effective, but at present time, infliximab has not received FDA clearance for this disease.[41–43] Patients started on TNFα agents require maintenance dosing, though early evidence suggests these agents do not necessarily reduce the frequency of new lesion development; however, discontinuation of the agent leads to new flares.[44] In addition to TNFα inhibitors, less established biologic therapies have demonstrated early promise, including IL-17 inhibition via ustekinumab and IL-1 inhibition via anakinra. Blok et al. reported 82% response rate in 17 patients treated with ustekinumab in an uncontrolled study, mirroring earlier results with the same agent.[45,46] Tzanetakou et al. demonstrated a 67% response rate to anakinra versus 20% in the placebo group in a clinical trial with 20 patients.[47] Antiandrogenic therapies may be beneficial as maintenance therapy.[48] Oral retinoids, including isotretinoin and acitretin, have mixed results, and their use is limited in a large population of HS patients (i.e. females of reproductive age).

These modalities, ultimately, are aimed at decreasing active inflammation, at which point patients are generally good candidates for more definitive surgical excision of the affected areas. The goal of surgical intervention is to prevent recurrence of inflammation in pre-existing tracts

0.pdf

Table 19.1 Diagnostic criteria to be used in primary care setting and by dermatologists [22]

Primary care setting Outbreaks of boils during the last 6 months with a minimum of two boils with five different location options [axilla, groin, genitals, under the breasts, and other locations, e.g., perianal, neck, and abdomen]
Dermatology clinic setting (a) Obligatory criteria • History: Recurrent painful or purulent lesions more than 2×/6 months • Location: Groin, armpit, perineum, buttock area, and submammary/intramammary fold (women) • Clinical signs: – *Primary lesions* Follicular papules/pustules (folliculitis), **nodules** (**inflammatory** or noninflammatory), **abscesses** , **tunnels** (**fistula/sinus**; **draining** or non-draining) – *Secondary lesions* Cysts, double pseudo-comedones, scars (atrophic, netlike, erythematous, hypertrophic, linear, or bridged) (b) Additional criteria (not obligatory) • History: HS-positive family history • Microbiology: No evidence of pathogens or presence of normal skin microflora at the predominant primary type of lesions
Diagnosis of HS if: • All three obligatory criteria are present • One or more obligatory locations are involved • One or more types of diagnostic lesions are present (**primary lesions in bold letters are diagnostic lesions**)

Table 19.2 International Hidradenitis Suppurativa Severity Score System (IHS4) [24]

IHS4 (*points*) =	
• Number of inflammatory nodules multiplied by 1 +	
• Number of abscesses multiplied by 2 +	
• Number of draining tunnels (fistulae/sinuses) multiplied by 4	
Mild HS	1–3 points
Moderate HS	4–10
Severe HS	11 or more points

Table 19.3 Hurley's clinical classification of HS [25]

Stage	Definition
I	Individual primary lesions and/or cysts without fistulae or scarring
II	Individual primary lesions and/or cysts with presence of fistulae and scarring
III	Confluent primary and secondary lesions at involved surface(s) with fistulae and scars

Table 19.4 Modified European guidelines for treatment [31]

I. Active (inflammatory) disease		
Mild	***Moderate–severe***	
Topical: Clindamycin 1%	Conventional systemic management: Clindamycin + rifampicin/tetracyclines/ acitretin	
	Treatment with biologics: Adalimumab (registered)/infliximab (off label)	
II. Inactive (noninflammatory) disease		
Hurley I	***Hurley II***	***Hurley III***
No surgery	Deroofing, lasers, local excision	Radical surgical excision (with secondary wound healing)
Adjuvant*:* Weight loss and tobacco abstinence (essential), pain management, treatment of superinfection		

19.3.1 Comorbid Disorders

Obesity, diabetes, hypertension, metabolic syndrome, dyslipidemia, depression, and substance dependence are often associated with HS [26], together with increased risk for cardiovascular diseases [27]. HS is also often associated with acne conglobata, dissecting cellulitis, and pilonidal sinus forming together a so-called follicular occlusion tetrad [1]. Further associations are those with inflammatory bowel conditions (Crohn's disease, ulcerative colitis), seronegative arthritis, and spondyloarthritis [28]. Co-occurrence of HS with Crohn's disease has been estimated in 0.6–38% and with ulcerative colitis in 14% of the cases. In contrast, only 0.8% HS patients also present Crohn's disease and 1.3% ulcerative colitis [29]. HS can also co-occur with pyoderma gangrenosum. Manifestations of HS with other genetic or acquired syndromes such as the *SAPHO syndrome*, *KID syndrome*, the *Dowling-Degos disease*, *steatocystoma multiplex*, *Sjogren syndrome*, and other rare entities have been reported [30].

19.4 Management

The treatment of HS is challenging for any physician since it requires a long-term strategy with consecutive measures together with careful monitoring. General therapeutic recommendations have been recently standardized in Europe including *topical*, *systemic*, and *surgical* measures, depending on the stage of the disease and the patient characteristics (Table 19.4). In mild cases topical agents such as 1% clindamycin, benzoyl peroxide, and 15% resorcinol peel may be successful to prevent or delay progression. Intralesional triamcinolone injections (2.5–10 mg/ml) in combination with oral and topical management act as an effective anti-inflammatory intervention in isolated HS nodules.

0.pdf

Table 20.10 Pharmacological and non-pharmacological treatment of hidradenitis suppurativa

- Local therapy
  - Benzoyl peroxide wash [125]
  - Topical clindamycin [129–131]
  - Topical resorcinol [132]
  - Intralesional corticosteroids [86]
- Systemic Therapy
  - Oral antibiotics
    - Tetracyclines
      - Doxycycline 50–100 mg BID
      - Minocycline 50–100 mg BID
    - Clindamycin 300 mg BID and rifampin 300–600 mg BID [105, 131, 133]
    - Dapsone 50–200 mg daily
  - Hormonal therapy
    - Anti-androgen medications i.e. cyproterone acetate + estrogen, oral contraceptives, oral contraceptives + spironolactone, finasteride
  - Targeted therapy
    - Infliximab [146, 147]
    - Adalimumab [104, 150]
    - Ustekinumab [153, 154]
    - Anakinra [155, 156]
    - Etanercept (not currently recommended) [151, 152]
  - Immunosuppressants
    - Systemic glucocorticoids [125]
    - Cyclosporine [140, 141]
    - Tacrolimus [157]
  - Oral retinoids
    - Acitretin 0.6 mg/kg daily for 9–12 months [143]
    - Isotretinoin 0.5–0.8 mg/kg for at least 4–6 months [136, 142]
  - Metformin [182]
  - Zinc supplementation [183, 184]
- Surgery
  - Punch debridement (mini-unroofing)
  - Incision and drainage [165]
  - Surgical unroofing
  - Carbon dioxide (CO_2) laser excision [167]
  - Wide excision [168, 169]
- Other procedures
  - 1064 nm long-pulsed Nd:YAG laser [158, 159]
  - Intense pulsed light [160]
  - External beam radiation [161]
  - Photodynamic therapy [162–164]

and finasteride are thought to be more effective than antibiotics alone [137–139, 144]. Oral contraceptive pills containing ethinyl estradiol or drospirenone are preferred and should be combined with spironolactone 50–100 mg if possible [145].

For severe, inflammatory HS, anti-TNFα inhibitors adalimumab and infliximab are associated with significant clinical improvement [104, 146–150]. Adalimumab is FDA (Food and Drug Administration) approved for moderate to severe HS. Infliximab appears to be more effective based on current evidence; however, more

THERAPEUTIC OPTIONS FOR HIDRADENITIS SUPPURATIVA	
Indication	**Treatment**
All Patients	**General Measures** • Weight reduction if obese or overweight • Measures to reduce friction and moisture 1. Loose undergarments 2. Absorbent powders 3. Antiseptic soaps 4. Topical aluminum chloride • Warm compresses • Stop smoking
Hurley Stage I Disease • Solitary or multiple isolated abscesses • No scarring or sinus tracts	**Medical Treatment** • Intralesional triamcinolone (5 mg/ml) injections into early inflammatory lesions • Topical clindamycin • Eradication of *S. aureus* carriage with topical mupirocin in nose, axillae, umbilicus, perianal regions • Oral antibiotics tailored to results of bacterial cultures from drainage discharge or abscess contents • Oral antibiotic therapy (alone or in combination) for its anti-inflammatory effect (tetracycline, doxycycline, minocycline, clindamycin, rifampin + clindamycin, dapsone, trimethoprim–sulfamethoxazole) • Oral anti-androgen therapy (e.g. finasteride)
Flares	• Short courses of systemic CS
Hurley Stage II Disease (see Fig. 31.11A) • Recurrent abscesses • Sinus tract formations • Early scarring	**Medical Treatment** • Systemic adjuvant or maintenance therapy (may be helpful in selected cases) 1. Acitretin 2. Infliximab 3. Cyclosporine **Surgical Treatment** • Limited local excisions with secondary intention healing • CO_2 laser ablation with secondary intention healing
Hurley Stage III Disease (see Fig. 31.11C) • Diffuse or broad involvement with multiple interconnected abscesses and sinus tracts • More extensive scarring	**Surgical Treatment** • Early wide surgical excision of involved areas • CO_2 laser ablation with secondary intention healing

Table 31.7 Therapeutic options for hidradenitis suppurativa.

For further information see Ch. 38. From *Dermatology, Third Edition*.

TABLE 84-4
Ratings of Select Therapies for Hidradenitis Suppurativa Based on Category of Evidence and Strength of Recommendation

THERAPY	CATEGORY OF EVIDENCE	STRENGTH OF RECOMMENDATION
First-line		
▪ Clindamycin (topical)[a]	IIb	Possible B
▪ Clindamycin/rifampicin (oral)[b]	III	C
▪ Adalimumab (subcutaneous)[c]	I	A
▪ Tetracycline (oral)	IIb	B
Second-line		
▪ Zinc gluconate	III	C
▪ Resorcinol (cream)	III	C
▪ Intralesional corticosteroid	IV	D
▪ Systemic corticosteroid	IV	D
▪ Infliximab	Ib/IIa	B
▪ Acitretin/etretinate	III	C
Third-line		
▪ Colchicine	IV	D
▪ Botulinum toxin (subcutaneous)	IV	D
▪ Isotretinoin	IV	D
▪ Dapsone	IV	D
▪ Cyclosporine	IV	D
▪ Hormones	IV	D
Surgery		
▪ Excision or curettage of individual lesions	III	C
▪ Total excision of lesions and surrounding hair-bearing skin	IIb	B
▪ Secondary intension healing	IIb	B
▪ Primary closure	III	C
▪ Reconstruction with skin grafting and negative pressure wound therapy	III	C
▪ Reconstruction with flap plasty	Ia/IIa	A/B
▪ Deroofing	IV	D
▪ CO_2 laser therapy	Ib	A
▪ Neodymium:yttrium-aluminum-garnet (Nd:YAG) laser	Ib	A
▪ Intense pulsed light	IV	D
Pain Control		
▪ Nonsteroidal antiinflammatory drugs	IV	D
▪ Opiates	IV	D
Dressings		
▪ No studies have been published as of this writing on the use of specific dressings or wound care methodology in hidradenitis suppurativa; choice of dressing is based on clinical experience	IV	D

[a]Single double-blind, placebo-controlled, randomized trial. Hurley stages I to II.
[b]Evaluated in case series.
[c]Multiple prospective, randomized, double-blind, placebo-controlled trials (Pioneer 1 and 2).
Adapted from Gulliver W, Zouboulis CC, Prens E, et al. Evidence-based approach to the treatment of hidradenitis suppurativa/acne inversa, based on the European guidelines for hidradenitis suppurativa. *Rev Endocr Metab Disord*. 2016;17(3):343-351, with permission.

TABLE 84-5
Category of Evidence/Strength of Recommendation Grading Scale

CATEGORY OF EVIDENCE	STRENGTH OF RECOMMENDATION
Ia: Metaanalysis of randomized controlled trials Ib: Randomized controlled trial	A: Category I evidence
IIa: Controlled study without randomization IIb: Quasiexperimental study	B: Category II evidence or extrapolated from category I evidence
III: Nonexperimental descriptive studies such as comparative, correlation, and case-control studies	C: Category III evidence or extrapolated from category I or II evidence
IV: Expert committee reports or opinion or clinical experience of respected authorities, or both	D: Category IV evidence or extrapolated from category II or III evidence

Data from Guyatt G, Oxman AD, Vist GE, et al. GRADE: An emerging consensus on rating quality of evidence and strength of recommendations. *BMJ*. 2008; 336:924; and from Gulliver W, Zouboulis CC, Prens E, et al. Evidence-based approach to the treatment of hidradenitis suppurativa/acne inversa, based on the European guidelines for hidradenitis suppurativa. *Rev Endocr Metab Disord*. 2016;17(3):343-351, with permission.

Kang_CH084_p1480-1494.indd 1488 07/12/1

0.pdf

Table 1 Spectrum of conditions associated with syndromic HS

Classification	Syndromes	Involved genes or chromosomal alterations
Group 1	Keratitis-ichthyosis-deafness syndrome (KIDS)	GJB2
	Down syndrome	Trisomy chromosome 21
	Dowling-Degos disease	KRT5 POFUT1, POGLUT1, and PSENEN
Group 2	Follicular occlusion syndrome	//
Group 3	Pyoderma gangrenosum, acne, suppurative hidradenitis (PASH)	MEFV, NOD2, NLRP3, IL1RN, PSTPIP1, PSMB8, NCSTN
	Pyogenic arthritis, pyoderma gangrenosum, acne, suppurative hidradenitis (PAPASH)	PSTPIP1, IL1RN, MEFV
	Psoriatic arthritis, pyoderma gangrenosum, acne, suppurative hidradenitis (PsaPASH)	//
	Pyoderma gangrenosum, acne, suppurative hidradenitis, ankylosing spondylitis (PASS)	//
	Familial Mediterranean fever (FMF)	MEFV
	Synovitis, acne, pustulosis, hyperostosis, osteitis (SAPHO)	LPIN2, NOD2, PSTPIP2, IL1RN

Abbreviations: *GJB2* Gap junction beta-2 protein, *IL1RN* interleukin-1 receptor antagonist, *KRT5* keratin 5, *LPIN2* lipin 2, *MEFV* Mediterranean fever, *NCSTN* nicastrin, *NOD2* nucleotide-binding oligomerization domain-containing protein 2, *NLRP3* NOD-, LRR-, and pyrin domain-containing protein 3, *POFUT1* protein O-fucosyltransferase 1, *POGLUT1* protein O-glucosyltransferase 1, *PSENEN* presenilin enhancer, *PSMB8* proteasome subunit beta type 8, *PSTPIP1* proline-serine-threonine phosphatase interacting protein 1, *PSTPIP2* proline-serine-threonine phosphatase interacting protein 2

- Group 1: syndromic HS associated with a genetic condition and related diagnostic testing – Dowling-Degos disease (DDD), Down syndrome (DS), keratitis-ichthyosis-deafness syndrome (KIDS), and PAPASH
- Group 2: syndromic HS associated with follicular keratinization disorders or structural disorders – follicular occlusion syndrome (FOS), DDD, DS, and KIDS
- Group 3: syndromic HS associated with autoinflammatory disease (monogenic, polygenic, other) – familial Mediterranean fever (FMF), PASH, PAPASH, PsaPASH, PASS, and SAPHO

In syndromic HS, a prevalent pathogenetic factor induces the follicular occlusion or a hyperactivation of the innate immune response, leading to the suppurative inflammation of the hair follicle. The diagnosis of syndromic HS is complex and should result from the combination of clinical evaluation (including HS-specific diagnostic criteria) (Fig. 1), histology of skin lesions (Fig. 2), laboratory findings, and genetic testing.

In the present chapter, we aimed at providing a comprehensive description of the main pathophysiological and clinical features of the following entities associated with HS belonging to the Group 3 of the classification by Gasparic et al., which are regarded as a paradigm of autoinflammatory syndromes: (i) PASH (pyoderma

0.pdf

8.20 Conclusion

Hidradenitis suppurativa is a very chronic and debilitating disease. The pain, discharge and chronicity have a severe psychological impact. The approach in management should consider all the factors and the molecules should be used judiciously. The targeted therapies like biologicals can help to improve quality of life and this option should be discussed with patient. The different modalities should be combined to achieve prolonged remission and attention should be given to the lifestyle modifications. Good counselling session, a sympathetic approach and appropriate use of various treatment modalities can help the patients to lead a near-normal life (Tables 8.1 and 8.2).

Clinical Results: (Figs. 8.7 and 8.8).

Table 8.1 Treatment Algorithm for HS [57, 58]

Hurley grade	Lifestyle modification	Medical management	Surgical and laser treatment
Mild-moderate	Weight reduction, cessation of smoking, loose clothes, antiseptic wash, pain management, psychological support	Topical clindamycin 1% for 12 weeks ILS for acute and recalcitrant lesions Zinc gluconate Doxycycline 100 mg bd	For both stationary and recurrent nodules and abscesses—Excision, CO_2 evaporation, drainage
Moderate to severe	Same as above	Oral clindamycin 300 mgm bd + rifampicin 300 mgm bd for 12 weeks Adalimumab for 12 weeks and evaluate or infliximab Other oral therapies Dapsone 25–200 mgm/day Acitretin 0.2–0.5 mgm/day Prednisolone 40–60 mgm per day and taper Cyclosporine 3–5 mgm/day	Deroofing of sinus tracts Excision of sinus tracts CO_2 laser Wide local excision plus second degree closure

0.pdf

Table 8.2 Medical management of HS

Mild localised	Mild widespread	Moderate	Severe
First line Topical treatment Clindamycin (1%) twice daily for 12 week (GRADE B) or Resorcinol (15%) once daily; twice daily for flares as needed (GRADE C) Second line Miscellaneous treatment for individual lesions such as intralesional triamcinolone (3–5 mg) one time, then repeated monthly if necessary (GRADE C)	First line Oral treatment Tetracycline (500 mg) twice daily for 12 week (GRADE B) or Doxycycline and minocycline (50–100 mg) twice daily (GRADE D)	First line Tetracycline (500 mg) twice daily for 12 week (GRADE B) or Doxycycline and minocycline (50–100 mg) twice daily (GRADE D) Second line Clindamycin + rifampicin combination for 10 week (GRADE B) Clindamycin (300 mg) twice daily Rifampicin (300 mg) twice daily Third line TNF-α inhibitor Adalimumab for 12 week followed by assessment (GRADE A) Loading doses Week 0 (160 mg subcutaneous) Week 2 (80 mg subcutaneous) Maintenance (40 mg subcutaneous) weekly or Infliximab (5 mg/kg intravenous) on weeks 0, 2 and 6, and then every 8 weeks thereafter (GRADE B) or Dapsone (25–200 mg) daily (GRADE C) or Acitretin (0.5 mg/kg) daily (GRADE C)	First line Clindamycin+rifampicin combination for 10 week (GRADE B) Clindamycin (300 mg) twice daily Rifampicin (300 mg) twice daily TNF-α inhibitor Adalimumab for 12 week followed by assessment (GRADE A) Loading doses Week 0 (160 mg subcutaneous) Week 2 (80 mg subcutaneous) Maintenance (40 mg subcutaneous) Weekly or Infliximab (5 mg/kg intravenous) on weeks 0, 2 and 6, and then every 8 weeks thereafter (GRADE B) Second line Immunosuppression for short treatment course Prednisone (40-60 mg) daily For 3–4 days then taper (GRADE C) or Cyclosporine (3-5 mg/kg) daily (GRADE C)

11 (48).png

nerapy, and genetic
lisposing factors.

rity of the diseases
than in nonsmoker
f smoking has not
disease.[23]

1.2 times for every
d to be more severe
. Few studies have
lic syndrome in HS
stress occurring in
essure and friction
ing factor.

een seen in more
nt inheritance.[11]
nt of chromosome
lished.[25]

ıd HLA-DR type
]

ciated with earlier

Table 3: Hidradenitis Suppurativa Physician Global Assessment Score

Score	Ratings	Description
0	Clear	No abscesses, no draining fistulas, no nodules
1	Minimal	No abscesses, no draining fistulas, no inflammatory nodules, presence of non-inflammatory nodules
2	Mild	No abscess or draining fistulas and <5 inflammatory nodules OR Single abscess or draining fistula and no inflammatory nodules
3	Moderate	No abscess or draining fistulas and <5 inflammatory nodules OR Single abscess or draining fistula in the presence of inflammatory nodules OR Between 2 and 5 abscesses or draining fistulas with or without inflammatory nodules, up to 10
4	Severe	Between 2 and 5 abscesses or draining fistulas with or without inflammatory nodules that greater than 10
5	Very severe	More than 5 abscesses or draining fistulas

0 (1).jpg

TABLE 158-1
Diagnostic Approach to Diseases That Produce Grains

DISEASE	ACTINOMYCOSIS	NOCARDIOSIS	ACTINOMYCETOMA	EUMYCETOMA	BOTRYOMYCOSIS
Clinical pattern	Lump with draining sinuses	Sporotrichoid, cellulitis, abscesses	Lump with draining sinuses	Lump with draining sinuses	Lump with draining sinuses
Site	Cervicofacial, thorax, abdomen, pelvic	Extremities (upper > lower)	Feet, back, extremities	Feet, mainly	Hand, head, feet
Source	Endogenous flora	Environment	Environment	Environment	Endogenous and environment
Most common agent	*Actinomyces israelii*	*Nocardia brasiliensis* *Nocardia asteroides*	*Nocardia brasiliensis* *Actinomadura madurae* *Actinomadura pelletieri* *Streptomyces somaliensis*	*Madurella mycetomatis* *Madurella grisea* *Pseudallescheria boydii*	*Staphylococcus aureus* *Escherichia coli* *Pseudomonas aeruginosa*
Grains, clinically or histologically	Common	Rare (only in disseminated cases)	Always	Always	Always
Grain contents	Filamentous bacteria	Filamentous bacteria	Filamentous bacteria	Hyphae	Cocci (most common)
Staining	Gram positive	Gram positive Weak acid-fast bacillus	Gram positive Weak acid-fast bacillus (only if *Nocardia*)	Periodic acid-Schiff, Grocott	Gram positive

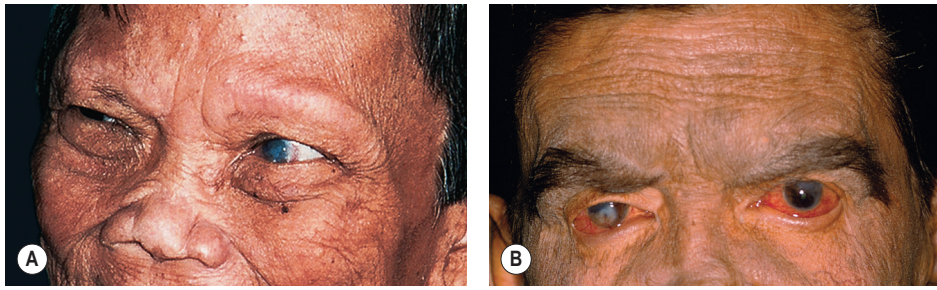


Fig. 62.6 Sequelae of leprosy. A The patient has madarosis, a saddle nose, and blindness in the left eye. **B** Ocular involvement and bluish discoloration of affected skin due to treatment with clofazimine. *A, Courtesy, Evangeline Handog, MD; B, Courtesy, Louis A. Fragola, Jr., MD.*

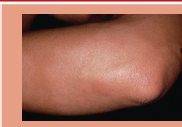
DIFFERENTIAL DIAGNOSIS OF LEPROSY		
Hypopigmented lesions		• Mycosis fungoides, including the hypopigmented variant • Sarcoidosis, but hypopigmented variant is usually more papulonodular • Postinflammatory hypopigmentation
Circinate (annular) plaques		• Mycosis fungoides and other forms of cutaneous lymphoma • Sarcoidosis • Psoriasis • Interstitial granulomatous dermatitis • Granuloma annulare • Tinea corporis
Infiltrated plaques/ nodules		• Lymphoma • Sarcoidosis • Other infections (dimorphic fungal, tuberculous) • For DDx of leonine facies, see Table 38.1
Neurologic findings		• Peripheral neuropathy due to other disorders (e.g. diabetes mellitus, vasculitis)
Deforming acral features		• Systemic sclerosis • Tabes dorsalis • Dupuytren's contracture
Type 1 reaction		• Acute lupus erythematosus • Cellulitis • Drug reactions • Misdiagnosed as worsening of disease as subclinical lesions may become apparent
Type 2 reaction		• Sweet's syndrome • Medium-vessel vasculitis • Panniculitides, e.g. erythema nodosum • Infections, including other mycobacterial, bacterial, dimorphic fungal, and other opportunistic fungal

Table 62.4 Differential diagnosis of leprosy.

0 (3).pdf

TABLE 159-1
Differential Diagnosis

Primary Lesions

- **Macules and patches.** The hypopigmentation of pityriasis alba and indeterminate leprosy mimic each other. If the patient was born in, or had resided in, an endemic area, then the distinction between the two may be made by neurologic or histologic examination. Hypopigmented BL plaques can be so faintly indurated as to mimic patches. Telangiectasias may be eruptive or present as mats on the face and upper trunk.
- **Papular to nodular lesions.** In the dermis, leprosy may mimic, or be mimicked, by dermatofibromas, histiocytomas, lymphomas, sarcoidosis, neurofibromatosis, syphilis, anergic leishmaniasis, paracoccidioidomycosis, chromoblastomycosis, sporotrichosis, lobomycosis, tuberculosis, and other granulomas. Eruptive and recurrent inflammatory subcutaneous nodules may be ENL, erythema nodosum, erythema induratum, and vasculitis. Palpable, but not visible, subcutaneous nodules in Lucio leprosy may mimic lipomas.
- **Plaques.** Erythematous plaques may mimic mycosis fungoides. Plaques without pigmentary change may be wheal like in appearance, causing confusion with urticaria. Hypopigmented plaques may mimic papulosquamous eruptions. Islands of normal skin within a plaque may suggest psoriasis.
- **Polymorphous vesiculobullous eruption/Dermoepidermal separation.** They may occur in ENL. IgM is deposited not uncommonly at the epidermal basement membrane in LL. These antibodies are not necessarily pathogenic but may confuse diagnosis.
- **Annular lesions.** Leprosy may mimic, or be mimicked by, annular erythemas, sarcoidosis, syphilis, or tinea.

Secondary Lesions

- **Infarcts.** Lucio phenomenon lesions and necrotic ENL mimic septic infarcts.
- **Ulcers.** Ulcers occur in Lucio phenomenon and ENL secondary to vascular occlusion. In patients with nerve destruction, neurotrophic ulcers occur on the plantar surface, patients with Leg ulcers secondary to venous insufficiency are seen in Lucio leprosy.

Clinical Constellations

- **Systemic lupus erythematosus–like changes.** Fusiform fingers, swan neck deformity, false positive syphilis tests, antiphospholipid antibodies, lupus anticoagulant, hyperglobulinemia, and anemia.
- **Vasculitis.** A true vasculitis may occur in ENL, Lucio phenomenon, and Lucio leprosy. Clinically, leprosy lesions of a nodular character may be misdiagnosed as "vasculitis."

CLINICAL COURSE AND PROGNOSIS

One of the most important problems during the leprosy clinical course is the appearance of acute or subacute episodes of inflammation, defined as reactions. Leprosy reactions, caused by immune response against *M. leprae* antigens, are divided into Type 1 or reversal reaction, involving mainly peripheral nerves and skin, and Type 2 or ENL, that may have localized or systemic symptoms. Acute neuritis also may be considered as a type of reaction.

Reactions never occur in Indeterminate patients. Up to 50% of all patients on multidrug therapy may present reactions during treatment, but these reactions can also occur before and after therapy. Neuropathy present at the time of diagnosis, multibacillary leprosy, extent of the disease, and the presence of lesions overlying peripheral nerve trunks are factors that increase the risk of reactions and nerve function impairment.[126] Reversal reaction and ENL may happen together in some patients (Table 159-2).

Reversal reaction can occur in up to 30% of patients, whereas tuberculoid leprosy cases are seldom affected,[127] the majority of the reactional episodes occur in borderline forms, mainly borderline-lepromatous and borderline-borderline, followed by lepromatous leprosy.[128] It starts as a sudden worsening of skin lesions and nerve function impairment, with no apparent systemic involvement. Besides prereactional lesions presenting more infiltration and desquamation, previous and newly developing lesions may be bright red, hot, and sensitive to the touch (Fig. 159-34), sometimes ulcerated, frequently associated with peripheral nerve enlargement, and usually accompanied by pain. Reversal reaction requires immediate intervention, because it can result in nerve impairment and permanent disabilities.

ENL is an aggressive vasculitis with immune complex deposition affecting different organs, resulting in, among other sequelae, neuritis, panniculitis, glomerulonephritis, arthralgia, epididymitis, orchitis, eye inflammation, osteitis and lymphadenitis with systemic symptoms such as fever, edema and malaise.[129]

TABLE 159-2
Lepra Reactions and Management

	REVERSAL REACTION (TYPE I)	ERYTHEMA NODOSUM LEPROSUM (TYPE II)
Predominant leprosy subtype	Borderline-tuberculoid Borderline-borderline Borderline lepromatous Lepromatous leprosy	Lepromatous leprosy
Signs and symptoms	Acute worsening of skin lesions Acute worsening of nerve function impairment No apparent systemic symptoms	Erythema nodosum Erythema polymorphous Severe cutaneous necrotizing vasculitis Fever, edema, malaise
Extracutaneous involvement	Neuritis	Neuritis Panniculitis Glomerulonephritis Arthralgia Epididymitis Orchitis Eye inflammation Osteitis Lymphadenitis
Treatment	Prednisone (1-2 mg/kg/d with slow taper ~3 mo)	Thalidomide 100-400 mg/d AND prednisone (1-2 mg/kg/d) OR Pentoxifylline 400 mg thrice a day

Kang_CH159_p2892-2924.indd 2914 04/12/

0 (105).png

Table 91.1 Characteristics of the different types of pemphigus

Disease	Antigen	Pathology	Immunofluorescence
Vulgaris	Desmoglein-3 (desmoglein-1)	Acantholysis in suprabasal layer	IgG, (C3), intercellular
Vegetans	Desmoglein-3 (desmoglein-1)	As above and papillomatosis, hyperplasia	IgG, (C3), intercellular
Neonatorum	Desmoglein-3 (PV)	As for PV	As for PV
Foliaceus, non-endemic	Desmoglein-1	Acantholysis in granular layer or subcorneal	IgG, (C3), intercellular
Brazilian endemic (fogo selvagem)	Desmoglein-1	As above	As above
Erythematosus	Desmoglein-1	As above	Intercellular IgG; C3 intercellular and granular at the basement membrane zone
Neonatorum	Desmoglein-3 (PV), desmoglein-1 (PF)	As for PV or PF	As for PV or PF
Paraneoplastic	Envoplakin, periplakin, 190-kDa protein, desmoglein-3, BP230, and others	Focal suprabasal acantholysis, dyskeratosis, basal vacuolization	IgG and C3 intercellular and fuzzy at the basement membrane
IgA-subcorneal pustular dermatosis	Desmocollin-1	Subcorneal pustules, intraepidermal acantholysis	Intercellular IgA in upper epidermis
IgA-intraepidermal neutrophilic dermatosis	Unknown	As above	As above

BP, bullous pemphigoid; PF, pemphigus foliaceus; PV, pemphigus vulgaris.

0 (106).png

Table 91.2 Characteristics of the different subepidermal blistering autoimmune diseases

Disease	Antigen	Pathology	Immunofluorescence
BP	BP230, BP180, 120 kDa protein, plectin	Subepidermal blister, mixed infiltrate with eosinophils	Linear n-serrated IgG, C3 BMZ; salt-split skin: epidermal site
MMP	BP180, laminin-332, integrin α6β4 (?),	Subepidermal blister, mixed mononuclear infiltrate, scarring	Linear n-serrated IgG, C3 BMZ; salt-split skin: epidermal site
Localized vulvar pemphigoid	BP230, BP180	Similar to BP	Linear n-serrated IgG, C3 BMZ; salt-split skin: epidermal site
Pemphigoid gestationis of the neonate	BP230, BP180	Similar to BP	Linear n-serrated IgG, C3 BMZ; salt-split skin: epidermal site
Epidermolysis bullosa acquisita and bullous SLE	Type VII collagen	Subepidermal blister; neutrophil-rich or minimal infiltrate	Linear u-serrated IgG, sometimes IgA, IgM, C3 BMZ; salt-split skin: deposits on dermal side
Linear IgA disease	120 kDa protein	Subepidermal blister; neutrophil-rich	Linear n-serrated IgA BMZ, salt on epidermal site
IgA-epidermolysis bullosa	Type VII collagen	Subepidermal blister; neutrophil-rich	Linear u-serrated IgA BMZ, salt
Dermatitis herpetiformis	Epidermal transglutaminsase	Subepidermal blister; neutrophil-rich	Granular IgA below BMZ

BP, bullous pemphigoid; BMZ, basement membrane zone; MMP, mucous membrane pemphigoid; SLE, systemic lupus erythematosus.

Box 87.3 Infections associated with blistering

Viral

- Herpes (herpes simplex, herpes varicella zoster), cytomegalovirus,
- Epstein–Barr virus, coxsackievirus, poxvirus (variola, monkeypox)

Fungal

- Candidiasis (neonatal cutaneous versus congenital)
- *Aspergillus*

Bacterial

- Gram-positive organisms
- *Treponema pallidum*
- *Staphylococcus* (impetigo neonatorum, SSSS)
- *Streptococcus* (particularly group B β-haemolytic)
- *Bacillus anthracis*
- *Listeria monocytogenes*
- Gram-negative organisms
- *Chlamydia trachomatis*
- *Escherichia coli*
- *Haemophilus influenzae*
- *Klebsiella pneumoniae*
- *Pseudomonas aeruginosa*

SSSS, staphylococcal scalded skin syndrome.

0 (108).png

ariants of EB
e. There are
rized by the
l distribution
cular defects.
vn as benign
ant mechano-
e of recurrent
cally involves
oin, inframa-
he neck, but

ant in infants
s gestationis

Box 87.6 Generalized blistering disorders

- Miliaria
  - miliaria crystillina
  - miliaria rubra
  - miliaria profunda
- EM
- Pustular psoriasis
- Urticaria pigmentosa
- Infections (see Box 87.3)

EM, erythema multiforme.

Box 87.8 Differential diagnosis of mucosal vesicles, erosions or pustules

Infections

- Herpes simplex virus
- Varicella virus
- Hand–foot–mouth disease
- Candidiasis

Inflammatory

- EM (Stevens–Johnson syndrome)
- TEN
- Oral aphthae

Autoimmune blistering diseases

- Chronic bullous disease of children
- Cicatricial pemphigoid
- Localized bullous pemphigoid

Genetic

- EB (junctional or dystrophic)

EM, erythema multiforme; EB, epidermolysis bullosa; TEN, toxic epidermal necrolysis.

Box 89.1 Systemic drugs used in the treatment of LAD with an indication as to their frequency

Commonly used	Dapsone [4,7,24,139,144]
	Sulphamethoxypyridazine [7,145]
	Sulphapyridine [4,7,20,23,25,145]
Occasionally used	Prednisolone [7,37,144]
	Azathioprine [7]
	Ciclosporin A (A. Anstey, personal communication, 1997)
Rare case reports	Colchicine [7,146,159,160]
	Oxacillin [56]
	Dicloxacillin [153,154]
	Erythromycin [156]
	Mycophenolate mofetil [161]
Historical	Arsenic [18,20,23]

The blistering is suppressed by dapsone or sulphonamides. Dapsone is the drug most commonly used, either alone or in combination. It was found to be effective in 42% of childhood LAD patients when used as single-agent therapy; 75% of children received dapsone as either single or combination therapy. The authors typically start

8.58 x 10.87 in
Options
976 of

0 (111).png

Table 4.2: Uses of direct immunofluorescence

Diagnosis	Deposit	Pattern	Site
Pemphigus	IgG	Fishnet (reticulate)	Intercellular
Bullous pemphigoid	IgG, C3	Linear	BMZ
Cicatricial pemphigoid	IgG (C3/IgM)	Linear	BMZ
Epidermolysis bullosa acquisita	IgG (C3/IgM)	Linear	BMZ
Dermatitis herpetiformis	IgA (C3)	Granular	Papillary dermis
Linear IgA dermatosis	IgA (IgG, C3)	Linear	BMZ
Lupus erythematosus	IgG, (C3, IgM)	Granular	BMZ
Henoch–Schönlein purpura	IgA	Granular	Vessel wall

BMZ: Basement membrane zone

is relatively expensive and its interpretation is time consuming

0 (112).png

Table 32.5: Classification of bullous disorders according to whether they are autoimmune or not

Immune-mediated bullous disorders

Intraepithelial blistering group of disorders

- Pemphigus and its variants

Subepidermal immune mediated disorders

- Bullous pemphigoid
- Mucous membrane pemphigoid
- Linear IgA bullous dermatosis
- Epidermolysis bullosa acquisita
- Pemphigoid gestationis
- Dermatitis herpetiformis

Bullous disorders without associated autoantibodies

Inherited

- Epidermolysis bullosa

Metabolic

- Porphyrias

Inflammatory

- Erythema multiforme
- Staphylococcal scalded skin syndrome
- Grover's disease

0 (113).png

Table 32.6: Classification of bullous disorders according to the morphology of lesions

Morphology of lesions	Disease
Flaccid bullae	Pemphigus and its variants, erythema multiforme, spongiotic dermatitis, staphylococcal scalded skin syndrome
Tense bullae	Bullous pemphigoid, cicatricial pemphigoid, dermatitis herpetiformis, porphyria, friction blister, diabetic bullae, epidermolysis bullosa acquisita, bullous lupus erythamatosus, viral infections, bullous impetigo, bullous mastocytosis, IgA bullous dermatosis, pemphigoid gestationis
Flaccid blisters and erosions	Pemphigus vulgaris
Superficial crusts	Pemphigus foliaceus, endemic pemphigus foliaceus
Vegetating lesions	Pemphigus vegetans
Polymorphous lesions	Paraneoplastic pemphigus
Vesicles and pustules	Dermatitis herpetiformis, dermatophytosis, viral infections, candidiasis, miliaria, subcorneal pustular dermatosis, erythema toxicum neonatorum, transient neonatal pustular melanosis, acropustulosis of infancy, incontinentia pigmenti, congenital syphilis, varicella, bullous congenital ichthyosiform erythroderma

0 (114).png

Table 32.8: Subepidermal blistering disorders and their associated BMZ antigens

Bullous disease	Target antigens
Epidermolysis bullosa simplex (muscular dystrophy)	Plectin
Herlitz junctional epidermolysis bullosa	Laminin 5
Junctional epidermolysis bullosa with pyloric atresia	Integrin α6β4
Non-Herlitz junctional epidermolysis bullosa	BPAg2 (BP180), laminin 5
Dystrophic epidermolysis bullosa	Type VII collagen
Bullous pemphigoid	BPAg1 (BP230), BPAg2 (BP180)
Cicatricial pemphigoid	BPAg2 (BP180), Epiligrin
Pemphigoid gestationis	BPAg2 (BP180)
Lichen planus pemphigoides	BPAg2 (BP180)
Linear IgA disease	BPAg2 (BP180)
Epidermolysis bullosa acquisita	Type VII collagen

that in the latter group the target antigens may be common to

Table 25.5: Classification of Bullous Disorders According to the Morphology of Lesions

Morphology of lesions	Disease
Flaccid bullae	Pemphigus and its variants, erythema multiforme, spongiotic dermatitis, staphylococcal scalded skin syndrome
Tense bullae	Bullous pemphigoid, cicatricial pemphigoid, dermatitis herpetiformis, porphyria, friction blister, diabetic bullae, epidermolysis bullosa acquisita, bullous lupus erythematosus, viral infections, bullous impetigo, bullous mastocytosis, IgA bullous dermatosis, pemphigoid gestationis
Flaccid blisters and erosions	Pemphigus vulgaris
Superficial crusts	Pemphigus foliaceus, endemic pemphigus foliaceus
Vegetating lesions	Pemphigus vegetans
Polymorphous lesions	Paraneoplastic pemphigus
Vesicles and pustules	Dermatitis herpetiformis, dermatophytosis, viral infections, candidiasis, miliaria, subcorneal pustular dermatosis, erythema toxicum neonatorum, transient neonatal pustular melanosis, acropustulosis of infancy, incontinentia pigmenti, congenital syphilis, varicella, bullous congenital ichthyosiform erythroderma

0.pdf

CLINICAL DIFFERENTIAL DIAGNOSIS OF LEPROSY	
Hypopigmented lesions	• Mycosis fungoides, including the hypopigmented variant • Sarcoidosis, but the hypopigmented variant is usually more papulonodular • Postinflammatory hypopigmentation
Circinate (annular) plaques	• Mycosis fungoides and other forms of cutaneous lymphoma • Sarcoidosis • Psoriasis • Interstitial granulomatous dermatitis • Granuloma annulare • Tinea corporis
Infiltrated plaques/nodules	• Lymphoma • Sarcoidosis • Other infections (e.g. dimorphic fungal infection, tuberculosis, leishmaniasis, syphilis) • For DDx of leonine facies, see Table 46.5
Neurologic findings	• Peripheral neuropathy due to other disorders (e.g. diabetes mellitus, vasculitis, nutritional disorders, syringomyelia)
Deforming acral features	• Systemic sclerosis • Tabes dorsalis • Dupuytren contracture
Type 1 reaction	• Acute cutaneous lupus erythematosus • Cellulitis and pseudocellulitis • Drug reaction • Misdiagnosis as worsening of disease when subclinical lesions become apparent
Type 2 reaction	• Sweet syndrome • Medium-vessel vasculitis • Panniculitides, e.g. erythema nodosum* • Infections, including other mycobacterial, bacterial, dimorphic fungal, and other opportunistic fungal

*Lesions favor the shins and are longer-lived than erythema nodosum leprosum lesions, which are widespread, appear in crops and then resolve relatively rapidly.

Table 75.4 Clinical differential diagnosis of leprosy.

peak serum concentrations, a longer serum half-life, and more bactericidal activity against *M. leprae* than does rifampin. In addition, moxifloxacin appears to be more bactericidal than ofloxacin. Thus, the combination of rifapentine, moxifloxacin, and minocycline (PMM) may be superior to rifampin, ofloxacin, and minocycline (ROM)[50].

For the two major inflammatory reactions, additional medications are often required. Oral prednisone (20–60 mg per day) is used for type 1 (reversal) reactions, while thalidomide (100–200 mg per day) is the principal therapy for type 2 reactions (erythema nodosum leprosum). Systemic corticosteroids are also recommended for the Lucio phenomenon. Although thalidomide remains the treatment of choice for type 2 reactions, teratogenicity is a major limitation and it is unavailable in many countries where leprosy is endemic. Lenalidomide and pomalidomide are thalidomide analogues with different side-effect profiles (e.g. more myelosuppression) that could have potential utility in the treatment of type 2 reactions. Additional drugs with possible benefit in type 2 reactions include cyclosporine, which has been used for corticosteroid-resistant type 1 reactions, as well as clofazimine, chloroquine, pentoxifylline, and phosphodiesterase type-4 inhibitors (e.g. roflumilast)[50,51].

Although leprosy is now considered a curable disease with a good prognosis and excellent survival rate, it can still be incapacitating and stigmatizing. It is very important to make the diagnosis as soon as possible and to examine contacts, since early treatment prevents disability. Recognition of leprosy in its initial phases by healthcare professionals as well as the general population in endemic countries is essential in order to reduce the impact of this disease[8].

CUTANEOUS TUBERCULOSIS

Key features

- Infection of the skin due to *Mycobacterium tuberculosis*, an acid- and alcohol-fast bacillus
- A resurgence of tuberculosis (TB) in the late 1980s and early 1990s resulted from the HIV epidemic, emergence of resistant strains of *M. tuberculosis*, and a decline in TB control efforts
- Exogenous exposure produces primarily the tuberculous chancre and TB verrucosa cutis
- Endogenous infection can lead to scrofuloderma, miliary TB, and lupus vulgaris
- Tuberculids include a papulonecrotic eruption, lichen scrofulosorum, and erythema induratum

MULTIDRUG THERAPY/WHO SCHEME FOR THE TREATMENT OF LEPROSY						
	Rifampin	Clofazimine	Dapsone	Ofloxacin	Minocycline	Therapy duration
MB (>5 lesions*)	600 mg once monthly	300 mg once monthly and 50 mg daily	100 mg daily	–	–	12 blister packs over 12 to 18 months
PB (2–5 lesions*)	600 mg once monthly	–	100 mg daily	–	–	6 blister packs over 6 to 9 months
PB (single lesion*)	600 mg × 1	–	–	400 mg × 1	100 mg × 1	Single dose
Dose adjustments for children						
10 to 14 years of age, MB†	450 mg once monthly	150 mg once monthly and 50 mg every other day	50 mg daily	–	–	12 blister packs over 12 to 18 months
<10 years of age, MB†	300 mg once monthly	100 mg once monthly and 50 mg twice weekly	25 mg daily	–	–	12 blister packs over 12 to 18 months
5 to 14 years of age, single lesion PB	300 mg × 1	–	–	200 mg × 1	50 mg × 1	Single dose

*WHO classification for endemic areas when no facilities for performing bacilloscopy are available.
†For PB disease (2–5 lesions), clofazimine is not required and the duration of therapy is 6 to 9 months.

Table 75.5 Multidrug therapy/WHO scheme for the treatment of leprosy. These recommendations are those currently standardized by the WHO[7,38,45–47]. MB, multibacillary; PB, paucibacillary.

Table 2-2: Differential Diagnosis for Diaper Dermatitis

Entity	Clinical Findings
Acrodermatitis Enteropathica *(Fig 2.4A-B)*	Erythematous crusted patches/plaques with flaccid bullae in perineal, periorificial, and distal extremities; due to ↓ **zinc level** (also ↓ **alkaline phosphatase** as zinc-dependent); may occur in following settings:
	1. **Premature** infants (poor absorption and ↑ requirement of zinc) when **weaned off breast milk** (which has adequate zinc level) 2. Inherited form (AR) manifests when **weaned off breast milk** 3. Healthy infants if low zinc level in maternal milk 4. Acquired form if malabsorption or inadequate nutrition
Allergic Contact Dermatitis	Rare in infants, ± related to topical preparations or foods
Atopic Dermatitis	Increased incidence of diaper dermatitis in atopic patients
Multiple Carboxylase Deficiency	Both resemble acrodermatitis enteropathica (periorificial dermatitis); treatment for both forms (listed below) is **biotin**
Biotin Deficiency	1. Neonatal form: AR, **holocarboxylase synthetase deficiency**, ± erythroderma with alopecia, fatal if not treated 2. Juvenile form: **biotinidase deficiency**, ± seizures, alopecia, hearing loss, developmental delay
Bullous Impetigo	Honey-colored crusts and flaccid bullae
Candidal Dermatitis *(Fig 2.3E)*	Bright red patches with pustules and satellite papules, ± intertriginous involvement **(including scrotum)**, ± thrush
Congenital Syphilis *(Fig 2.3B-D)*	Reddish-brown papulosquamous eruption, may be **erosive or bullous**
Cystic Fibrosis	Resembles acrodermatitis enteropathica, also due to zinc deficiency ± pedal edema, failure to thrive, infections and malabsorption
Granuloma Gluteale Infantum	Red to violaceous granulomatous nodules over the vulva, perianal area, buttocks, ± scrotum; due to irritation, occlusion, candidal infection
Irritant Dermatitis	Poorly-demarcated erythematous plaques, **spares inguinal folds**
Kawasaki Disease	Tender erythema in perineal area which later desquamates
Langerhans Cell Histiocytosis *(Fig 2.3F)*	Yellow-brown crusted papules with purpura in **seborrheic** distribution; ± systemic involvement; Langerhans cells **(CD1a +, S100+)**
Miliaria	Clear vesicles or erythematous papules/pustules due to blocked eccrine ducts from heat or humidity in diaper area
Perianal Pseudo-verrucous Nodules	Erythematous nodules and papules in children with fecal incontinence
Perianal Strep	Bright red, well-demarcated perianal erythema and involving creases
Psoriasis	Sharply-demarcated bright pink to red plaques **involving inguinal creases**, minimal scale; most common psoriatic presentation in infants
Scabies	Erythematous nodules involving diaper area, ± genitalia
Seborrheic Dermatitis	Typical salmon-covered scaly patches and plaques involving the scalp, groin and other intertriginous areas

Diaper Dermatitis

Table 22 Diaper dermatitis – potential etiologies and symptoms

Type	Symptoms
Irritant dermatitis	Diaper-covered surfaces, spares folds Chronic wetness, increased pH, diarrhea
Candidal dermatitis	**Bright red**, moist patches with satellite pustules Intertriginous involvement of thrush
Seborrheic dermatitis	Groin, scalp, intertriginous areas Salmon colored, waxy scaling patches, and plaques
Psoriasis	Well-demarcated, pink plaques with minimal scale, creases involved Most common presentation of psoriasis in infants
Acrodermatitis Enteropathica/zinc deficiency	Brown, orange crusted plaques with vesicles and bullae Perineal, perioral areas, and distal extremities 2° to low serum zinc level 1.) Premature infants: poor absorption, inadequate stores, and ↑ zinc requirement 2.) Healthy infants: low breast milk zinc levels with normal maternal serum zinc level 3.) Acquired form: malabsorption and/or inadequate nutritional intake (i.e., TPN) 4.) Autosomal recessive inherited form: defect in intestinal zinc-specific transporter SLC39A4 that manifests when infant is weaned off breast milk (due to greater availability of zinc maternal breast milk than non-maternal source) Alkaline phosphatase (zinc-dependent enzyme) also low **Make sure lab uses non-zinc containing tube (special collection tube).**
Langerhans cell histiocytosis (Letterer–Siwe Disease)	Yellowish-brown, crusted papules with **petechiae** in a seborrheic distribution CD1+, S100+ Langerhans cells with comma-shaped or reniform nuclei. Multisystem involvement may be present
Jacquet's erosive dermatitis	Severe erosive papules, nodules. May cause pain with urination **Multifactorial etiology**: yeast, irritant dermatitis, and moisture
Granuloma gluteale infantum	Red-purple, granulomatous nodules 2° local irritation, maceration and *Candida* (multifactorial)
Allergic contact dermatitis	Topical preparations or foods
Cystic fibrosis	Resembles zinc deficiency Pedal edema common Failure to thrive, hepatosplenomegaly, infections, malabsorption

(continued)

Table 22 (continued)

Type	Symptoms
Biotin deficiency/multiple carboxylase deficiency	Resembles zinc deficiency but affects all biotin-dependent enzymes *Neonatal form*: AR holocarboxylase synthetase – vomiting *Juvenile form*: AR biotinidase – optic atrophy and hearing loss *All*: seizures (6 months of age), hypotonia, ataxia, lactic acidosis/ketosis, hyperammonemia, alopecia Treatment → biotin lifelong
Perianal streptococcal Disease	**Bright red**, well-defined erythema perianally and in creases
MRSA	Increasingly common – may see nodules/abscess
Bullous impetigo	Flaccid bullae with honey-colored crusts
Miliaria	Blocked eccrine ducts secondary to heat and humidity of diaper area. May be superficial, small, clear vesicles (miliaria crystalline) or small, erythematous papules/pustules (miliaria rubra/ miliaria pustulosa)
Scabies	Lesions tend to be more nodular under the diaper
Kawasaki's Disease	2/3 of patients present with **confluent**, **tender erythema in perineum**. Later → desquamates
Congenital syphilis	Condyloma lata or generalized papulosquamous eruption of secondary syphilis may be present in diaper area
Perianal pseudoverrucous Papules and Nodules	Erythematous flat-topped papules and nodules in children with chronic fecal incontinence
Human immunodeficiency virus (HIV)	Very severe erosive diaper dermatitis. May be complicated by secondary bacterial and viral infections

Table 1: Differential diagnosis of diaper area rash

Disease	Characteristic feature	Diagnosis
Dermatoses primarily related to wearing diaper		
Irritant contact dermatitis	Sparing of the creases - gluteal and groin fold	Clinical
Candidal diaper dermatitis	Satellite papules and pustules involve the groin fold	KOH
Milaria	Can involve other parts of the body - neck, face, fold/creases of the body History of using warm clothes or fever	Clinical
Granuloma gluteal infantum	Reddish, brown papules to nodules Arises in areas of preexisting diaper dermatitis	Clinical, skin biopsy
Pseudoverrcous plaques and papules	Multiple red moist flat-topped papules and nodules in the gluteal and diaper area	Clinical, skin biopsy
Dermatoses exaggerated by wearing diaper		
Seborrhic dermatitis	Involved fold, erythema, and greasy scales Other site involvement - cradle cap and behind ear	Clinical
Atopic dermatitis	Involves mainly convex areas History of atopy	Clinical
Psoriasis	Involves convex areas and the groin fold	Clinical. Skin biopsy
Dermatoses in diaper area - not related to diaper wearing		
Langerhans histiocytosis	Discrete yellowish papules, purpuric atrophic or ulcerated in seborrheic distribution	Skin biopsy
Acrodermatits entropathica	Sharply demarcated psoriasiform plaques, vesicles, and bullae Location - periorificial and acral Associated with diarrhea, irritability, alopecia	Serum zinc levels - <50 μ/dL
Bullous impetigo	Vesicles, papules with crusting over the periorificial region	Clinical, gram stain, culture
Molluscum contagiosum	Discrete umblicated papules	Clinical, KOH
Hand foot and mouth disease	Discrete papules and vesicles over hand, foot, gluteal, genital, oral cavity	Clinical
Genital warts	Verrcous papules to plaques - perianal area Should raise a suspicion of child sexual abuse	Clinical, skin biopsy
Scabies	Papules, nodules, excoriation over palms and soles, genitals	Clinical, wood's lamp, scraping positive for mites, eggs

Flowchart 1 gives an algorithm on how to approach a case of diaper rash.

Methods

This hospital-based observational, prospective study was Conducted for a period of 8 months from January 2022 to August 2022. All children below 5 years of age with eruptions involving the diaper area presenting to the Department of Pediatric Dermatology at the Indira Gandhi Institute of Child Health, Bengaluru, Karnataka, were enrolled in the study. Informed written consent was obtained from the caregivers. We calculated the required sample size to be 67, based on the prevalence of DD to be 22.3%.[1] A detailed history, including recent infections, history of allergies, family history, general physical examination, and dermatological examination, We're done and recorded in a predesigned proforma. Appropriate clinical and laboratory tests such as Tzanck smear, skin biopsy, KOH examination, swab for culture sensitivity, Gram staining, and hematological investigations were done whenever necessary.

Data were compiled in Microsoft Excel and were analyzed using statistical software R version 4.2.1. Categorical variables were given in the form of frequency tables. Continuous variables were given in mean ± SD/median (minimum–maximum) form. Chi-square test was used to check the association between categorical variables.

Results

A total of 135 children Under the age of 5 presenting with lesions on the diaper area were enrolled in the study. Hospital-based prevalence of DD was 3.4%. The age of the study population ranged from 12 days to 5 years, with a mean age of 1.46 ± 1.35 years. The majority of the cases were infants aged between 28 days and 1 year (72/135, 53.3%), followed by toddlers whose ages ranged between 1 and 3 years (44/135, 32.5%),

absorbent core was composed primarily of cellulose fluff. During that time, several conflicting studies compared the incidence of diaper dermatitis in infants using cloth diapers versus infants using disposable diapers.[32] In the mid-1980s, a superabsorbent core material was developed. It was composed of a cross-linked sodium polyacrylate that transforms to hold a proportionately large amount of fluid within a gel substance. Several studies have concluded that superabsorbent diapers are superior to cloth diapers in preventing diaper dermatitis.[32] In addition, superabsorbent diapers may prevent occult fecal contamination of clothing and fomites in daycare settings.[33] Another diaper innovation was first marketed in 2000 as Pampers Rash Care diapers. An incorporated inner layer continuously deposits a petroleum-based barrier product to the skin. Limited trials with normal infants demonstrated a reduction in skin microtopography and erythema when compared with controls.[34] These diapers can be quite effective at preventing and helping to heal diaper rashes, but the downside is they are expensive when compared with other diapers on the market. There have been reports of allergic contact dermatitis to various blue, pink, and green dyes used in the production of diapers. Dye-free diapers should be used for allergen avoidance if necessary.[35] Routine use of topical preparations to prevent diaper dermatitis is not necessary for infants with normal skin. Some of these products have additional risks. Additives have the potential to cause contact sensitization, irritation and/or percutaneous toxicity. Powders applied vigorously enough to aerosolize pose an aspiration risk. This is especially true for talc (mainly hydrous magnesium silicate) powders which can cause irritant pneumonitis. Talc may also cause granulomatous reactions when applied to wounds. Contrary to previous theory, cornstarch does not enhance the growth of *C. albicans* on the skin.[36] Boric acid, once popular as a diaper rash treatment and still an ingredient in some diaper care products, is a cause of diarrhea, erythroderma and failure to thrive.[3] A new product containing a combination of miconazole, zinc oxide, and white petrolatum was recently released on the market, Vusion (Barrier Therapeutics, Inc. Princeton, NJ). It is indicated for the treatment of candida diaper dermatitis, but is costly. It also contains fragrance, a potential allergen.

Appropriate treatment of diaper dermatitis begins with correct diagnosis of the underlying cause. Most infants develop acute diaper dermatitis as a result of the factors described above. However, other primary pathologic processes must be considered for any infant with chronic, severe and/or recurrent diaper rash. Primary cutaneous diseases that may present with diaper rash include contact dermatitis, seborrheic dermatitis, psoriasis and candidiasis. Infants with atopic dermatitis may be more susceptible to irritants, and diaper dermatitis was common in this group prior to the availability of superabsorbent diapers. Since that time, the diaper area of atopic infants is most often dramatically spared, an important diagnostic and therapeutic sign. Several uncommon causes of diaper dermatitis have serious, or even life-threatening, implications[37] (Box 4.1). These conditions should always be considered in infants presenting in the first month of life, in immunocompromised patients and in those who are not otherwise thriving.

BOX 4.1 UNCOMMON CAUSES OF DIAPER DERMATITIS

- Acrodermatitis enteropathica
- Bullous pemphigoid
- Cutaneous signs of child abuse – ecchymoses, scald injury
- Chronic bullous dermatosis of childhood
- Congenital syphilis
- Cystic fibrosis
- Dermatitis herpetiformis
- Ecthyma gangrenosum
- *Enterobius* (pinworm) infestation
- Epidermolysis bullosa
- Granuloma gluteale infantum
- Herpes simplex
- Langerhans cells histiocytosis
- Immunodeficiency syndromes
- Inborn errors of metabolism
- Incontinentia pigmenti
- Kawasaki disease
- Papular urticaria
- Perianal streptococcal dermatitis
- Post-scarlet fever desquamation
- Psoriasis
- Scabies
- Staphylococcal scalded skin syndrome
- Tinea inguinalis
- Wiskott–Aldrich syndrome.

Modified from Schaad et al. (1991)[38] with permission.

Mild to moderate irritant diaper dermatitis should be treated initially by reminding caregivers of the importance of avoiding excessive wetness and exposure to feces. This can be achieved with traditional frequent diaper changes and the use of superabsorbent diapers. Leaving the area open is impractical and use of a hair dryer may cause inadvertent injury. All potential irritants or sensitizers, including often-overlooked commercial diaper wipes, should be discontinued. Water-dampened soft cloths or paper towels, or mineral-oil-soaked cotton pledgettes are safe

32. Lane A, Rehder P, Helm K. Evaluation of diapers containing absorbent gelling material with conventional disposable diapers in new-born infants. *Am J Dis Child.* 1990;144:315.
33. Rory V, Wun C, Morrow A, et al. The effect of diaper type and overclothing on fecal contamination in day-care centers. *JAMA.* 1991;265:1840.
34. Odio MR, O'Connor RJ, Sarbaugh F, et al. Continuous topical administration of a petroleum formulation by a novel disposable diaper. 1. Effect on skin surface microtopography. 2. Effect on skin condition. *Dermatology.* 2000;200:232–234.
35. Alberta L, Sweeney SM, Wiss K. Diaper dye dermatitis. *Pediatrics.* 2005;116:e450–e452.
36. Leyden J. Corn starch, *Candida albicans,* and diaper rash. *Pediatr Dermatol.* 1984;1:322.
37. Lane A. Diaper rash: causes and cures. *Patient Care.* 1988;22:167–173.
38. Schaad UB, Stoupis C, Wedgwood J, et al. Clinical, radiologic and magnetic resonance monitoring for skeletal toxicity in pediatric patients with cystic fibrosis receiving a three-month course of ciprofloxacin. *Pediatr Infect Dis.* 1991;10:723.

BOX 14.7 DIFFERENTIAL DIAGNOSIS OF AN ERUPTION IN THE DIAPER REGION

Inflammatory
- Irritant diaper dermatitis
- Allergic contact diaper dermatitis
- Jacquet's diaper dermatitis
- Granuloma gluteale infantum
- Intertrigo
- Perianal pseudoveruccous papules and nodules (PPPN)
- Seborrheic dermatitis
- Atopic dermatitis
- Psoriasis

Infectious
- Candidiasis
- Folliculitis (*Staph. aureus*)
- Perianal streptococcal disease
- Bullous impetigo

Nutritional
- Acrodermatitis enteropathica (zinc deficiency)
- Essential fatty acid deficiency
- Biotin deficiency
- Kwashiorkor secondary to malabsorption
- Cystic fibrosis
- Langerhans cell histiocytosis

skin conditions occurring under the diaper. Diaper rashes are among the most common skin conditions seen in infancy. Most diaper rashes occur as a direct result of wearing diapers and are referred to as irritant diaper dermatitis. Rarely, there is true allergic contact dermatitis to diapers. Primary cutaneous disorders such as psoriasis and seborrheic dermatitis frequently occur under the diaper and tend to be worsened by the occlusive properties of the diaper. Systemic disorders, such as acrodermatitis enteropathica and Langerhans cell histiocytosis, occur independently of the wearing of the diaper and may mimic irritant diaper dermatitis. Disorders of the gastrointestinal tract such as cystic fibrosis, celiac disease and inflammatory bowel disease often produce perineal eruptions as well as other inflammatory, infectious, nutritional, and malignant conditions as listed in Box 14.7.

HISTORY OF DIAPERING

The term diaper dermatitis includes all eruptions that occur in the area covered by the diaper. These conditions are caused directly by the wearing of diapers (irritant contact dermatitis), those that are aggravated by diapers (e.g., psoriasis), and those that occur whether or not diapers are worn (e.g., acrodermatitis enteropathica).[375] In many societies where diapers are not worn, infants escape a condition that is commonly seen in pediatric practice in more industrialized countries.[376]

The first true description of diaper dermatitis was made by Jacquet in 1905,[377] although Parrott described a lesion in the diaper area in 1887.[378] In 1915, Zahorsky described the frequency of diaper eruptions associated with an 'ammoniacal' smelling diaper.[379] In Great Britain in the 1970s, diaper dermatitis accounted for 20% of all skin consultations in the 0- to 5-year age group,[380] and in Japan, the prevalence varied between 6% and 50%, depending on definitions and inclusion criteria.[381–383] Since the advent of newer diapering practices, mainly the introduction of disposable diapers with super-absorbent gel centers, the figure has dropped considerably.[384] Nevertheless, mothers in the USA still frequently consult pediatricians for diaper eruptions.[385]

Diapers have only gained widespread acceptance in the Western world during the last 70 years, with the appearance of the modern diaper in the 1920s. These have evolved through using pieces of cloth and safety pins, to the 1930s, when diaper services became widely available, and more recently to disposable diapers that have been used extensively in the last 40 years.[376] There are three methods of diapering utilized in most countries. Parents can buy ready-made cloth diapers and launder them at home. With this method, there is a residue of chemicals left in the diaper despite numbers of rinses. It is the most common cause of irritant diaper dermatitis (IDD) in infants. Major problems in the past have arisen from antiseptics used in laundering.[386,387] Quaternary ammonium compounds are now the most common chemical used in the laundering of home diapers.

A diaper service is another method of diapering. Diaper services usually provide their customers with their own new diapers, that are collected weekly or bi-weekly. They are cycled through as many as 11 hot rinses, the first seven being with detergents. Two or more diapers may be used simultaneously, increasing the absorbency. The diapers are usually covered with a plastic pant.

Disposable diapers were first used in the 1960s and have become increasingly refined. They have changed from paper, to an absorbable cellulose center, to the most modern diapers, which have a super-absorbent gel center carrying wetness from

375. Koblenzer PJ. Diaper dermatitis: an overview. *Clin Pediatr*. 1973;12:386.
376. Levin S. History of medicine-diapers. *S Afr Med J*. 1970;44:256–263.
377. Jacquet L. Traité des maladies de l'enfance. In: Grancher J, Comby J, Marfan AB, eds. Paris: Masson & Co; 1905:714.
378. Boisits EK, McCormack JJ. Diaper dermatitis and the role of predisposition. In: Maibach HI, Boisitis EK, eds. *Neonatal skin; structure and function*. New York: Marcel Dekker; 1982:191.
379. Zahorsky J. The ammoniacal diaper in infants and young children. *Am J Dis Child*. 1915;10:436.
380. Verbov JL. Skin problems in children. *Practitioner*. 1976;217:403–415.
381. Berg RW. Etiology and pathophysiology of diaper dermatitis. *Adv Dermatol*. 1988;3:75–90.
382. Jordan WE, Lawson KD, Berg RW, et al. Diaper dermatitis frequency and severity among a general infant population. *Pediatr Dermatol*. 1986;3:198–201.
383. Longhi F, Carlucci G, Bellucci R, et al. Diaper dermatitis: a study of contributing factors. *Contact Derm*. 1992;26:248–252.
384. Wong DL, Brantly D, Clutter LB, et al. Diapering choices: a critical review of the issues. *Pediatr Nurs*. 1992;18:41–54.
385. Krowchuk DP. Characterization of diaper dermatitis in the United States. *Arch Pediatr Adolesc Med*. 2000;154:943–946.
386. Brown BW. Fatal phenol poisoning from improperly laundered diapers. *Am J Public Health*. 1970;60:901.
387. Jensen JPA. Transcutaneous absorption of boron from a baby ointment used prophylactically against diaper dermatitis. *Nord Med*. 1971;86:1425–1429.

Table 19.2 (continued)

Nature of the lesion	Main causes
Raynaud's phenomenon	Aicardi-Goutieres syndrome Angiocentric lymphoma Anorexia nervosa Autoimmune diseases: scleroderma, mixed connective tissue disease, lupus erythematosus, dermatomyositis (particularly antisynthetase syndrome), rheumatoid arthritis, etc. Buerger's disease Cannabis-induced arteritis Cold agglutinin-induced disease Cryoglobulinemia, cryofibrinogenemia Drugs and toxic products: polyvinyl chloride, silicone implant, bleomycin, interferon, cyclosporin, COX-2 inhibitors + APL, cocaine, snake bite, etc. Ergotism Hypereosinophilic syndrome Mechanical causes: thoracic outlet syndrome, carpal tunnel syndrome Neurovascular instability syndrome Raynaud's disease Vascular form of acrokeratosis paraneoplastica Vascular form of multiple sclerosis Virus infections: HIV, parvovirus B19, etc.
Erythermalgia	Connective tissue diseases Drugs Gout Idiopathic Multiple sclerosis Myeloproliferative syndrome Neuropathies, including of small fibers Thrombotic thrombocytopenic purpura Vasculitis

CMV cytomegalovirus, *EBV* Epstein-Barr virus, *HIV* human immunodeficiency virus

Erythema

Acute erythema should suggest an infectious disease such as staphylococcal toxic shock syndrome or Kawasaki disease but also erysipeloid or infection with *Streptococcus iniae*, as well as other inoculation diseases.

Toxic causes should not be forgotten (mercury, chemotherapy), as well as metabolic and paraneoplastic causes (acrokeratosis paraneoplastica, necrolytic acral erythema of glucagonoma) and chronic viral infections (HIV, HCV [hepatitis C virus]).

In connective tissue diseases, hands are often affected, particularly in lupus erythematosus and dermatomyositis.

Phlebitis and lymphedema are more edematous than erythematous.

Common

Physiological, pregnancy, cirrhosis

Raynaud's Phenomenon

In case of unilateral Raynaud's phenomenon, a compression (thoracic outlet syndrome, carpal tunnel syndrome) should be suspected. If bilateral, toxic causes, connective tissue diseases, and cryopathies must be searched for, and the possibilities of acrokeratosis paraneoplastica and polymyositis, which are often hallmarked by a severe Raynaud's phenomenon, not forgotten.

Common

Raynaud's disease

19.3 Diaper Rash

Examination should specify:

- Topography: friction area, perianal, and predominance in folds
- Associated lesions: papules, erosive and/or crusted papules that should suggest Langerhans cell histiocytosis, pustules that are common in candidiasis, collarette scaling suggesting candidiasis or necrolytic migratory erythema, and bullae (congenital syphilis)
- General signs

Box 19.1 Main Causes of Diaper Rash in Infants

Allergic contact dermatitis (diapers, topical products)
Atopic dermatitis
Candidiasis
Dermatitis herpetiformis
Dermatophytosis
Ecthyma gangrenosum
Gianotti-Crosti syndrome (infantile papular acrodermatitis)
Gluteal granuloma
Irritant dermatitis (contact, "systemic": tooth eruption)
Jacquet's erosive diaper dermatitis (or syphiloid post-erosive pyodermitis of Sevestre and Jacquet)
Kawasaki disease (involvement of the buttocks is common, but there are always associated signs)
Langerhans cell histiocytosis
Necrolytic migratory erythema (enteropathic acrodermatitis)
Psoriasis (napkin psoriasis)
Seborrheic dermatitis (Leiner-Moussous)
Staphylococcal scalded skin syndrome (affection can be predominant on the buttocks, with typical superficial skin detachment)
Streptococcal anitis

19.4 Scrotal Erythema/Edema

Box 19.2 Main Causes of Scrotal Erythema/Edema

Anasarca
Acute urinary retention
Crohn's disease
Erysipela
Fournier's gangrene
Glucagonoma syndrome
Idiopathic scrotal edema in children
Inflammatory flare-up of lymphedema
Neoplastic lymphangitis
Zinc deficiency, vitamin B2 (riboflavin) deficiency, etc.

Do Not Miss

Some certain serious diseases can manifest as intertrigo: Langerhans cell histiocytosis, glucagonoma syndrome, and pemphigus. Primary HIV infection can manifest as an intertrigo. Simultaneous affection of several folds is characteristic of a particular form of drug eruption.

Common

Maceration (particularly submammary and abdominal folds), atopic dermatitis, bacterial intertrigo, dermatophytosis, candidiasis, and psoriasis

19.5 Intertrigo

Box 19.3 Main Causes of Intertrigo

Amicrobial pustulosis of the folds
Bacterial intertrigo
Candidiasis
Contact dermatitis and atopic dermatitis
Crohn's disease[a]
Darier's disease
Dermatophytosis
Endogenous eczema and drug eruptions ("SDRIFE")
Erythrasma
Fox-Fordyce's disease[a]
Granular parakeratosis
Hailey-Hailey disease
Hereditary mucoepithelial dysplasia
Hidradenitis suppurativa (acne inverse or Verneuil's disease in the French terminology)
Hyperimmunoglobulin E syndrome (Job syndrome)
Inflammatory adenopathies[a]
Inflammatory apocrine adenocarcinoma[a]
Irritation, maceration
Langerhans cell hystiocytosis[a]
Lichen (planus)
Mycosis fungoides (granulomatous slack skin)
Necrolytic migratory erythema in glucagonoma syndrome, enteropathic acrodermatitis, and related disorders
Olmsted syndrome
Paget's disease[a]
Pemphigus vegetans
Primary HIV infection
Pseudoxanthoma elasticum[a]
Psoriasis
Subcorneal pustulosis of Sneddon-Wilkinson and IgA pemphigus
X-linked ectodermal dysplasia with immunodeficiency (hypomorphic mutations in IKBKG)

[a]Lesions are preferentially located in folds and are not necessarily erythematous; other primary lesions may be associated to erythema: papules, plaques, vesicles, and pustules

TABLE 3.1.4 DIAPER DERMATITIS CONTINUED

Type	Symptoms
Perianal pseudoverrucous papules and nodules	Erythematous flat-topped verrucous papules and nodules in children with chronic fecal incontinence Brown, orange crusted plaques with vesicles and bullae. Perineal, perioral areas, and distal extremities
Acrodermatitis enteropathica/ zinc deficiency	Secondary to low serum zinc level 1. Premature infants: Poor absorption, inadequate stores, and increased zinc requirement 2. Healthy infants: Low breast milk zinc levels with normal maternal serum zinc level 3. Acquired form: Malabsorption and/or inadequate nutritional intake (i.e., total parenteral nutrition) 4. Autosomal recessive inherited form: Defect in intestinal zinc-specific transporter SLC39A4 that manifests when infant is weaned off breast milk (due to greater availability of zinc in maternal breast milk than nonmaternal source) Alkaline phosphatase (zinc-dependent enzyme) also low
Langerhans cell histiocytoses (LettererSiwe disease)	Yellowish-brown, crusted papules with petechiae in a seborrheic distribution $CD1a^+$, $S100^+$ Langerhans cells with comma-shaped or reniform nuclei. Multisystem involvement may be present
Granuloma gluteale infantum	Red-purple, granulomatous nodules Secondary to local irritation, maceration, and Candida (multifactorial)
Allergic contact dermatitis	Topical preparations (or foods rarely); dyes
Cystic fibrosis	Resembles zinc deficiency Pedal edema common Failure to thrive, hepatosplenomegaly, infections, malabsorption
Biotin deficiency/multiple carboxylase deficiency	Resembles zinc deficiency, but affects all biotin-dependent enzymes Neonatal form: Autosomal recessive; holocarboxylase synthetase; vomiting Juvenile form: Autosomal recessive; biotinidase; optic atrophy and hearing loss All: Seizures (6 mo of age), hypotonia, ataxia, lactic acidosis/ketosis, hyperammonemia, alopecia. Treatment: Biotin lifelong
Atopic dermatitis	Uncommon primary cause of diaper dermatitis, but patients with atopic dermatitis at increased risk of diaper dermatitis
Miliaria	Blocked eccrine ducts secondary to heat and humidity of diaper area. May be superficial, small, clear vesicles (miliaria crystallina) or small, erythematous papules/pustules (miliaria rubra/miliaria pustulosa)
Scabies	Lesions tend to be more nodular under diaper
Kawasaki's disease	Two-thirds of patients present with confluent, tender erythema in the perineum. Later desquamates
Congenital syphilis	Condylomata lata or generalized papulosquamous eruption of secondary syphilis may be present in diaper area
Human immunodeficiency virus	Very severe erosive diaper dermatitis. May be complicated by secondary bacterial and viral infections

Figure 3.1.4 Erythema toxicum neonatorum.

Figure 3.1.5 Seborrheic dermatitis.

BOX 17.1 CAUSES OF DIAPER DERMATITIS

INFLAMMATORY CONDITIONS

- Irritant diaper dermatitis
- Seborrheic dermatitis
- Atopic dermatitis
- Psoriasis
- Psoriasiform diaper dermatitis with id reaction
- Erosive perianal eruption
- Pseudoverrucous papules
- Granuloma gluteale infantum
- Senna-induced blistering after laxative ingestion
- Allergic contact dermatitis due to diaper components
- Diaper dye dermatitis and 'Lucky Luke' dermatitis

INFECTIONS

- Candidiasis
- Bullous impetigo/staphylococcal scalded skin syndrome
- Perianal streptococcal dermatitis/streptococcal intertrigo
- *Pseudomonas*/ecthyma gangrenosum
- Tinea infection
- Herpes simplex infection
- HPV infection (condylomata)
- Molluscum contagiosum
- Coxsackie viral infection (hand, foot, and 'butt' exanthem)

METABOLIC

- Nutritional abnormalities
- Zinc deficiency
- Acrodermatitis enteropathica
- Acrodermatitis enteropathica-like eruptions
  - Methylmalonic acidemia
  - Propionic acidemia
  - Glutaric aciduria (type 1)
  - Maple syrup urine disease
  - Ornithine transcarbamylase deficiency
  - Citrullinemia
  - Biotin deficiency
  - Holocarboxylase deficiency
- Cystic fibrosis

MISCELLANEOUS

- Langerhans' cell histiocytosis
- Kawasaki disease
- Granular parakeratosis
- Pyramidal perianal protrusion
- Nascent hemangioma
- Lichen sclerosus
- Pyoderma gangrenosum
- Chronic bullous disease of childhood
- Bullous pemphigoid

in disposable diapers include a slow-release petrolatum surface and a breathable outer sheet.

The most important factor in preventing IDD is the frequency and number of diaper changes. Other factors causing IDD include episodes of diarrhea, antibiotic use, and anatomical problems such as short bowel syndrome. Whereas cloth diapers are less efficient at reducing skin wetness, friction and pH, there is a risk that the expense of superabsorbable diapers may prevent parents from changing the diaper sufficiently often, thus contributing to the development of IDD.

Cutaneous findings

IDD presents as erythema on the convex surfaces of the inner upper thigh, the lower abdomen, and buttock areas, the areas most in contact with the diaper. The creases and the suprapubic area in boys are spared (Fig. 17.1). The eruption may become more severe and inflammatory, with yeast colonization, and

Figure 17.1 Irritant diaper dermatitis with characteristic sparing of the folds.

Figure 17.2 (A) Jaquet's dermatitis. Well-demarcated, punched-out erosions, and ulcers primarily on convex surfaces.

enlarging areas of involvement, including the creases. In more severe cases, the erythema may be accompanied by a glistening or glazed appearance and a wrinkled surface.

Jacquet's erosive dermatitis presents with well-demarcated punched-out ulcers and erosions (Fig. 17.2A,B). It is seen less commonly with the use of disposable diapers, and has usually been associated with infrequent diaper changes and poor removal of chemicals used in home laundering. It may also be seen in infants who have short bowel syndrome or following surgery for Hirschsprung disease, which may result in chronic diarrhea.

Etiology and pathogenesis

At birth, a newborn's skin undergoes a sudden transition accompanied by drying and cooling of the skin surface as it adapts to its new environment.[7] Visscher[8] has measured the changes in the newborn's epidermal barrier properties over the first 4 weeks of life, showing increased surface hydration, less transepidermal water movement under occlusion, and a decrease in surface pH. Diapered and non-diapered sites are indistinguishable at birth, but over the first 2 weeks of life diapered areas show consistently increased pH and hydration, thus setting the stage for IDD.

TABLE 16-1 The differential diagnosis of diaper area eruptions

Disease	Usual age	Skin: morphology	Skin: usual distribution	Clinical:other	Method of diagnosis/ findings
Eruptions where the diaper/diaper environment is a central cause					
Irritant diaper dermatitis (IDD)	Between 3 weeks and 2 years. Peak ages 9–12 months	Erythema, with fine scaling and glazed skin surface. Erosions and ulcerations when severe	Convex surfaces of upper inner thigh, lower abdomen and buttock; spares intertriginous creases	Risk factors: cloth diapers, diarrhea	Clinical
Erosive perianal eruption	Usually infants 6 weeks to 3 months of age	Well demarcated erosions and superficial ulcerations 0.5–1.5 cm	Perianal skin, opposing areas of buttocks	Associated with frequent stooling of any etiology	Clinical
Pseudoverrucous papules	Usually infants rather than newborns	Well demarcated dome-shaped papules 2–10 mm, with shiny, smooth red or white surface	Perianal region, buttocks, vulvar, scrotal or around enterostomal openings	Severe, intractable diarrhea from any cause- short gut syndrome, following surgery for imperforate anus or pull through for Hirschsprung disease. May mimic condylomata clinically	Usually Clinical Biopsy shows reactive acanthosis or psoriasiform spongiotic dermatitis
Granuloma gluteale infantum	Usually infants rather than newborns	Oval red-brown to violaceous dermal papules or nodules 5 mm to 2–3 cm. Lesions run parallel to skin lines	Perianal, perivulvar or gluteal surfaces of the diaper region. Rarely inguinal folds, neck and axillae	Usually a history of chronic diaper eruption treated with multiple products, including fluorinated steroids	Clinical Biopsy shows dense superficial and deep inflammatory infiltrate composed of lymphocytes, histiocytes and plasma cells, proliferation of dermal blood vessels and extravasated red blood cells and hemosiderin
Granular parakeratosis	Usually 9–22 months of age	Asymptomatic, geometric, yellow brown, scaling plaques with underlying erythema	Areas of friction and pressure in diaper region. May involve axillae	None	Clinical Biopsy shows abnormal keratinization and retention hyperkeratosis
Infantile seborrheic dermatitis (ISD)	First 4–6 weeks of life, but any time in the first year	Erythematous, well demarcated patches involving the creases; may affect entire diaper region. Scale often minimal in diaper region	Multiple areas may be involved especially scalp, eyebrows, sides of nose, axillae, chest and diaper region	Generally happy babies, unlike infants with AD who have more pruritus	Clinical KOH to r/o associated Candidiasis
Psoriasis	Under 2 years	Brightly erythematous, well demarcated patches and plaques typically with absent or thin white scale	Often starts on convex surfaces, may affect entire diaper region including creases, gluteal cleft; may also involve face, scalp, trunk, and umbilicus	Eruption often asymptomatic and unresponsive to usual diaper dermatitis treatments	Clinical +/- Skin Biopsy Epidermal Acanthosis, parakeratosis dilated capillaries

TABLE 16-1 The differential diagnosis of diaper area eruptions—cont'd

Disease	Usual age	Skin: morphology	Skin: usual distribution	Clinical:other	Method of diagnosis/ findings
Candidal diaper dermatitis with psoriasiform Id	Usually infants 6–24 months but may occur earlier	Initial candidal diaper rash with erythematous patches and peripheral satellite papules or pustules with associated papules and scaly plaques elsewhere on body	Typical (usually severe) eruption diaper area followed by rapid onset of papules and plaques involving the torso, face, less prominent on extremities	Usually asymptomatic; occasionally pruritic	Clinical KOH + psuedohyphae and spores in diaper region early on
Allergic contact dermatitis	Usually after 6 months of age	Erythema and small vesicles leading to area of eczematous eruption of red papules and vesicles overlying areas of edema	Depends on contact allergen involved: diaper dye dermatitis at margins of diaper Entire diaper region if due to applied topical products	Associated pruritus	Clinical Biopsy shows spongiotic dermatitis with eosinophils
Infectious causes					
Candidiasis	Common after 2 months of age	Beefy-red eruption emanating from folds with satellite pustules or erythematous eruption extending over perineum with peripheral scale	Begins in inguinal folds, may involve entire perineum	Often history of preceding antibiotic use or diarrhea preceding eruption. May have associated oral thrush	Clinical KOH and Culture positive for Candida
Impetigo	Often in first few weeks of life in diaper region	Single or multiple flaccid bullae or moist superficial erosions	Often starts in umbilical stump; spreads to intertriginous areas of diaper region	Usually no other symptoms but neonates with hematogenous spread may develop septicemia, osteomyelitis or septic arthritis	Clinical Gram stain, Culture Biopsy rarely required but shows subcorneal pustule
Perianal/perineal streptococcal dermatitis	Usually after 6 months of age more common in toddlers	Moist, bright red erythema around perianal skin with yellowish sticky exudates at periphery. May have small pustules in surrounding skin	Perianal skin most common but can be in inguinal creases, other body folds	Local pain and tenderness common, fever rare. May have concomitant streptococcal pharyngitis. May be trigger for guttate psoriasis	Clinical Culture positive for B-Hemolytic Streptococci
Ecthyma gangrenosum	Usually seen in very premature or immunocompromised infants	Erythematous macule that rapidly evolves into grey nodule, necrotic bulla or ulceration with surrounding bright red areola	May occur anywhere but 50% occur in perineal/gluteal area	Associated neutropenia common. May rarely occur in diaper region in normal infants	Clinical gram stain and culture of lesions or + blood culture
Diaper dermatophytosis	Usually seen in toddlers	Erythematous scaling papules and plaques with border in diaper region. Deeper follicular papules and pustules in chronic cases	Buttocks, thighs and lower abdomen but may involve entire diaper area	Often family history of tinea pedis or other tinea infection	Clinical KOH and culture + For dermatophyte usually T. rubrum or T. Mentagrophytes
Herpes simplex	Presents 2–8 days after contact with infected individual	Grouped 2–3 mm umbilicated vesicles and erosions on erythematous base	Neonatal HSV may present on buttocks after breech delivery	Fever and regional adenopathy	Clinical + HSV culture or DFA or PCR. + tzanck smear of base of vesicle

TABLE 16-1 The differential diagnosis of diaper area eruptions—cont'd

Disease	Usual age	Skin: morphology	Skin: usual distribution	Clinical:other	Method of diagnosis/ findings
Condylomata acuminata	Usually seen through vertical transmission from an infected mother; incidence in young infants from child abuse unknown but low	1–3 mm flesh-colored papules that may coalesce to form plaques. Verrucous to velvety surface	May occur on any part of the perineum	Usually asymptomatic	Clinical HPV serotyping available
Molluscum Contagiosum	Rare in neonates, increasingly common in toddlers and early childhood	Umbilicated flesh colored or pink papules, usually several, occasionally large numbers	Often in folds or areas of friction	May have associated molluscum dermatitis	Clinical or biopsy if diagnostic uncertainty
Coxsackie Viral Infection	1–4 yrs of age	Small red macules that rapidly evolve into superficial ovoid vesicles on hands and feet. Small papules and superficial erosions seen over buttocks and thighs	Hand, foot and 'butt' (diaper area) exanthem with erosions and vesicles of buccal area, tongue, gingiva and anterior tonsillar pillars	Fever and malaise Rarely, encephalitis, aseptic meningitis, myocarditis Enterovirus 71 cases pulmonary hemorrhage	Clinical Viral culture
Eruptions with accentuation in diaper area irrespective of presence of diapers/diaper environment					
Zinc deficiency/ acrodermatitis enteropathica	True genetic AE occurs within 3 months after weaning; Zn deficiency common in breastfed premature infants within 1–2 months of age	Crusted, scaling, eczematous to psoriasiform dermatitis Face and diaper area	Periorificial, perineum, acral and periungual areas	Irritability, diarrhea, sparse hair, recurrent candidal infections especially paronychia, failure to thrive	Clinical Low serum Zinc Low Alkaline Phosphatase
Cystic fibrosis	Infancy	Periorificial and truncal dermatitis	Similar to AE	Significant edema, diarrhea, irritability, alopecia, failure to thrive	Clinical Sweat chloride test CFTR mutational analysis
Langerhans' cell histiocytosis	Birth to 4 years	Single, few or multiple lesions; Morphology may vary: yellow-brown papules, nodules, vesicles, erosions, ulcerations, atrophy, palpable petechial lesions, purpura, scale or crusting either alone or in combination	Folds of diaper region characteristic, also trunk scalp and retrauricular regions	Gums teeth and nails may be involved. Bony involvement in 50%; lymphadenopathy 14%; Liver or CNS in 10% (diabetes insipidus)	Clincal confirm with Skin biopsy showing infiltrate of CD1A + cells in epidermis and dermis
Pyramidal perianal protrusion	Usually 1–30 months of age	Pyramidal shaped soft tissue 'tag-like' protrusion – occasionally has a tongue-like lip	Seen in midline of perineum typically anterior to the anus but can be at other locations.	Often a history of constipation or diarrhea. May be associated with lichen sclerosus	Clinical Biopsy shows normal skin unless LS changes present (rarely required)
Nascent ulcerated infantile hemangioma	Birth to a few days of life	Oval to annular area of superficial to full thickness skin ulceration. Often surrounding telangiectasia or tiny vascular papules	Perianal, perivulvar and buttocks, may occur on lip or perioral region	Associated pain, occasionally secondary infection. Concern for spinal dysraphism/ urogenital anomalies with very large lumbosacral lesions	Clinical- hemangioma becomes evident over next few days to weeks. Biopsy: Glut-1 + vessels

TABLE 16-1 The differential diagnosis of diaper area eruptions—cont'd

Disease	Usual age	Skin: morphology	Skin: usual distribution	Clinical:other	Method of diagnosis/ findings
Lichen sclerosus	Usually in childhood 5–7 yrs, but may be seen in infancy	White, glistening, atrophic changes in the vulvar area and perianal skin. Associated purpura, and small hemorrhagic vesicles may be seen	Figure-of-eight distribution in perineum. Phimosis in boys; rarely extragenital lesions	Associated pain, itching, dysuria constipation and encopresis may be present	Clinical Biopsy confirms (rarely necessary)
Pyoderma gangrenosum	Uncommon in infancy but reported as young as 3 months	Tender papulopustule rapidly evolves into undermined ulcer with violaceous border. Rarely bullous and hemorrhagic	Head and anogenital sites most common in infants and children. Lower extremities in older children	Painful, usually associated with IBD, also seen in immunodeficiency, Leukocyte adhesion defect, leukemia, rheumatic disorders	Clinical Biopsy not specific but helpful to exclude other disorders ie infectious ulcers and vasculitis
Chronic bullous disease of childhood	Usually in early childhood Rare in infancy	Annular to polycyclic vesicles and bullae forming rosettes or 'string of pearls'	Diaper area, buttocks and inner thighs characteristic with spread to the trunk and scalp and face	May present initially with fever or other constitutional symptoms	Clinical Confirm with biopsy-subepidermal blister with polys and eosinophils Immunoflourescence + Linear IgA deposits
Bullous pemphigoid	Rare in infants and children but earliest reported case 2 months of age	Urticarial papules and plaques evolve into tense, often hemorrhagic bullae 0.25–2 cm in size. Blisters on normal or inflamed skin	Widespread distribution, often involves perineum, flexures of limbs and face mucosal involvement may occur in older children	Associated itching and pain	Clinical Confirm with biopsy-subepidermal Blister with eosinophils Immunoflourescence-deposits of C_3, And IgG at BMZ
Kawaski disease	Infancy to 5 yrs	Eruption may be polymorphous; often involves diaper region in young infants, with perineal erythema, small sterile pustules, urticarial lesions, early evidence of desquamation in perineal area	Accentuation perineal area but can be widespread macular erythema, urticarial, scarlatiniform, or maculopapular lesions	Persistent fever, irritability conjunctivitis, strawberry tongue, fissured lips, cervical adenopathy, peripheral edema, leukoocytosis, thrombocytosis, increased ESR, sterile pyuria, pericardial effusions and myocarditis	Diagnostic Clinical Criteria Echocardiogram

Extracutaneous Findings

None.

Etiology/Pathogenesis

At birth a newborn's skin undergoes a sudden transition accompanied by drying and cooling of the skin surface as it adapts to its new environment.[7] Visscher[8] has measured the changes in the newborn's epidermal barrier properties over the first 4 weeks of life, showing increased surface hydration, less transepidermal water movement under occlusion, and a decrease in surface pH. Diapered and nondiapered sites are indistinguishable at birth, but over the first 2 weeks of life diapered areas show consistently increased pH and hydration, thus setting the stage for IDD.

IDD results from the interaction of several factors associated with prolonged contact of the skin with a combination of both urine and feces (Table 16.1). The wearing of diapers causes a significant increase in skin wetness and pH.[9] Prolonged wetness leads to maceration of the stratum corneum due to disruption of the intercellular lipid lamellae.[10]

eac (1).png

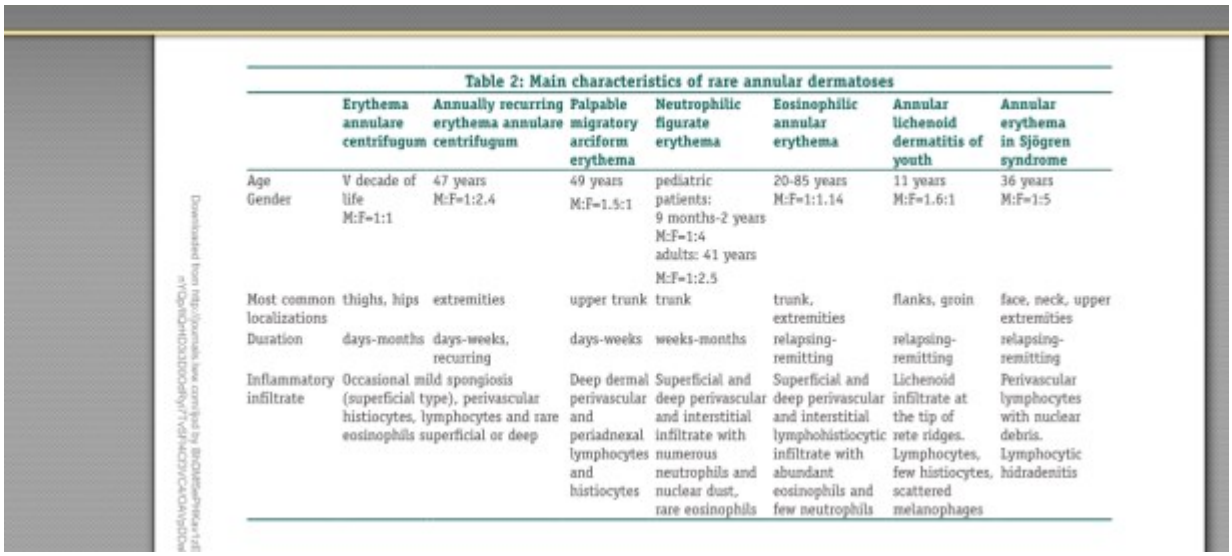


Table 2: Main characteristics of rare annular dermatoses

	Erythema annulare centrifugum	Annually recurring erythema annulare centrifugum	Palpable migratory arciform erythema	Neutrophilic figurate erythema	Eosinophilic annular erythema	Annular lichenoid dermatitis of youth	Annular erythema in Sjögren syndrome
Age	V decade of life	47 years	49 years	pediatric patients: 9 months-2 years	20-85 years	11 years	36 years
Gender	M:F=1:1	M:F=1:2.4	M:F=1.5:1	M:F=1:4 adults: 41 years M:F=1:2.5	M:F=1:1.14	M:F=1.6:1	M:F=1:5
Most common localizations	thighs, hips	extremities	upper trunk	trunk	trunk, extremities	flanks, groin	face, neck, upper extremities
Duration	days-months	days-weeks, recurring	days-weeks	weeks-months	relapsing-remitting	relapsing-remitting	relapsing-remitting
Inflammatory infiltrate	Occasional mild spongiosis (superficial type), perivascular histiocytes, lymphocytes and rare eosinophils superficial or deep		Deep dermal perivascular and periadnexal lymphocytes and histiocytes	Superficial and deep perivascular and interstitial infiltrate with numerous neutrophils and nuclear dust, rare eosinophils	Superficial and deep perivascular and interstitial lymphohistiocytic infiltrate with abundant eosinophils and few neutrophils	Lichenoid infiltrate at the tip of rete ridges. Lymphocytes, few histiocytes, scattered melanophages	Perivascular lymphocytes with nuclear debris. Lymphocytic hidradenitis

Downloaded from http://journals.lww.com/ by BhDMf5ePHKbH4TlCutT3kC7f/Vnt2JCD8vNQZ05fLWo1gnXvlNeG8qEepZwBveEg3thAbKdioB1zYJIC3X4Q1Iu7pppGbabbSrlch4o3jXkJADJx79pNRq1zvsXwX8AWWohY4FoZVFJiJiM7KKUpPOb4a3d2qNc/IMfbPoA==

Table 1: Exosome sources in development

Category	Subcategory	Examples	Description	Therapeutic potential
Conventional	Human/mammal	Lymphocytes, dendritic cells, epithelial cells, endothelial cells, mast cells, neurons, blood, saliva, urine, breast milk, amniotic fluids, hydrothoracic fluids, ascitic fluid	Traditional source of exosomes	Insights into basic physiological processes and potential therapeutic applications
Nonconventional	Animal product derived	Milk, honey, royal jelly, bee pollen, venom	*Apis mellifera* royal jelly extracellular vesicles demonstrated to modulate mesenchymal stem cell differentiation and secretome, and decrease lipopolysaccharide-induced inflammation in macrophages by blocking the mitogen-activated protein kinase pathway	Promote synthesis and reconstruction of stratum corneum lipids, enhance skin barrier function, and provide greater protection for the skin Anti-inflammatory properties to reduce skin irritation, and antioxidant activity, slowing down the skin ageing process
				Antibacterial properties
				Exhibit biofilm-inhibiting effects and promote stem cell migration
			Increase migration of human dermal fibroblasts	Therapeutic applications in wound healing and tissue regeneration
			Snake venom extracellular vesicles (EVs) found rich in 5′ nucleosidase, L-amino acid oxidase, serine proteases, and metalloproteinases	Use described in mucositis, colitis, bone formation, and infected ulcers or diabetic foot ulcers
	Bacterial, fungal, and parasitic	*C. neoformans, H. capsulatum, P. brasiliense, Leishmania spp, Plasmodium spp, Toxoplasma spp, Lactobacillus spp, Akkermansia muciniphila, Phellinus linteus*	EVs modulate the innate immune responses	Lipid bilayer of bacterial EV experimented for potential drug delivery
				Increased re-epithelialization and angiogenesis
				Antifungal vaccines
				Inhibition of ultraviolet-induced skin ageing
				Immunomodulatory therapy for malignancy, metabolic diseases, and immune/ inflammatory diseases
	Fruit flies and nematodes	*D. melanogaster, C. elegans*	Involved in developmental processes and possibly adult behaviours	Scar remodelling, senescence, and wound recovery
	Lower vertebrates, molluscs	Salmon, zebrafish, frogs	Related to development and disease responses	Skin regeneration and repair
				Scar reduction
				Improving skin texture and elasticity
	Plant-derived exosomes	Pollen, seeds, fruits	Similar in size and function to mammalian exosomes	Proliferation of human fibroblasts
				Reduce melanin synthesis
				Hair regeneration
	Wheat		Promote wound healing and skin regeneration by increasing collagen expression and vascular formation	Wound healing and skin regeneration therapies
	Transgenic plant-derived virus-like agents		Being explored for vaccine production	Ongoing clinical trials for plant-derived influenza vaccines

Table 19.3 Jakinibs approved for clinical use and those under investigation for skin disease

Drug	Manufacturer	Target	Status and use
First-generation Jakinibs			
Tofacitinib (CP690550)	Pfizer	JAK3>JAK1>>(JAK2)	FDA approved—RA
			Phase III—psoriasis, PsA, UC
			Phase II—AS, JIA, CD
Ruxolitinib (INC424)	Incyte/Novartis	JAK1, JAK2	FDA approved—PV, myelofibrosis
			Phase II—psoriasis, AD, AA, vitiligo, various malignancies
Baricitinib (LY3009104)	Incyte/Eli Lilly	JAK1, JAK2	Under FDA review—RA
			Phase II—psoriasis, AD, SLE
Oclacitinib (PF03394197)	Zoetis	JAK1	FDA approved—canine allergic dermatitis
Second-generation Jakinibs			
Lestaurtinib (CEP-701)	TEVA	JAK2, FLT3	Phase III—AML (FDA approved under orphan drug status)
			Phase II—myelofibrosis, PV, ET, psoriasis
Peficitinib (ASP015K)	Astellas/Maruho	JAK1>JAK3>>JAK2	Phase III—RA
			Phase II—psoriasis
Solcitinib (GSK2586184)	Galapagos/GlaxoSmithKline	JAK1	Phase II—psoriasis, SLE
Upadacitinib (ABT-494)	Abbvie	JAK1	Phase III—RA, UC
			Phase II—CD, AD
Itacitinib (INCB039110)	Incyte	JAK1>JAK2	Phase II—RA, psoriasis, chronic pruritus, various malignancies
			Phase I—GVHD
PF-04965842	Pfizer	JAK1	Phase II—psoriasis, AD

Abbreviations: *RA* rheumatoid arthritis, *PsA* psoriatic arthritis, *UC* ulcerative colitis, *AS* ankylosing spondylitis, *JIA* juvenile idiopathic arthritis, *CD* Crohn's disease, *PV* polycythemia vera, *ET* essential thrombocytosis, *GVHD* graft versus host disease, *AA* alopecia areata, *AD* atopic dermatitis, *SLE* systemic lupus erythematosus, *FLT3* Fms-like tyrosine kinase 3, *AML* acute myeloid leukemia, *MDS* myelodysplastic syndrome, *NSCLC* non-small cell lung cancer

is a concern with systemic Jakinibs given the wide-reaching effects of potent signal modulation of multiple type I and II cytokines. Minor variations in the kinase domain of JAKs allow for more directed targeting, but often there is considerable cross-reactivity between Jakinibs and their intended JAK target. The first-generation Jakinibs (tofacitinib, ruxolitinib, baricitinib, and oclacitinib) demonstrate more broadly targeting effects, whereas second-generation Jakinibs are somewhat more specific (Table 19.4).

Tofacitinib

Tofacitinib is among the first of the Jakinibs put into clinical use. Initially designated for RA, it is now in trials for numerous other autoinflammatory conditions such as inflammatory bowel disease (IBD), psoriatic arthritis (PsA), juvenile idiopathic arthritis (JIA), ankylosing spondylitis (AS), and psoriasis.

Tofacitinib blocks JAK-STAT signaling by functioning as a reversible, competitive inhibitor at the ATP binding site on JAK, effectively inhibiting autophosphorylation and autoactivation [41]. JAK3 is preferentially targeted, but inhibitory effects are also seen with JAK1 and to a lesser extent with JAK2 while TYK2 is minimally affected [42]. IL-6 signaling through STAT1/3/5 is also attenuated [42, 43]. Broad downstream effects are seen in muted T_H1 and T_H17

Table 19.4 Jakinib selectivity indexed to their most selective receptor (IC_{50} values [nM][a])

Drug	JAK1	JAK2	JAK3	TYK2
First-generation Jakinibs				
Tofacitinib [101] (CP690550)	6 (3)	2 (1)	1 (0.5)	22 (11)
Ruxolitinib [102] (INCB018424)	1 (3.3)	1 (2.8)	153 (428)	7 (19)
Baricitinib [103] (LY3009104)	1 (6)	1 (6)	67 (>400)	9 (53)
Oclacitinib [104] (PF03394197)	1 (10)	2 (18)	10 (99)	8 (84)
Second-generation Jakinibs				
Lestaurtinib [7] (CEP-701)	4 (8.8)	2 (3.7)	1 (2.3)	7 (15)
Peficitinib [74] (ASP015K)	5 (3.9)	7 (5)	1 (0.71)	7 (4.8)
Solcitinib [82] (GSK2586184)	1 (9.8)	11 (107.8)	55 (539)	23 (225.4)
Upadacitinib [78] ABT-494	1 (8, 40[b])	75 (600)	58 (2300[b])	–
Itacitinib (INCB039110)	–	–	–	–
PF-04965842	–	–	–	–

[a]Most IC_{50} data taken from in vitro cellular assay testing which may not accurately reflect in vivo receptor interactions and selectivity

[b]Extrapolated data based on ~58-fold higher IC_{50} in JAK1 versus JAK3 using a biochemical assay (40 nM and 2300 nM, respectively) compared to ~75-fold higher IC_{50} in JAK1 versus JAK2 from a cellular assay (8 nM versus 600 nM) [78]

in moderate-to-severe AA (14). However, topical formulations are still in development or early trials, aiming to reduce systemic side effects while maintaining efficacy (15).

Safety data so far are reassuring but warrant caution. Across trials, most treatment-emergent adverse events were mild or moderate (upper respiratory infections, nasopharyngitis, headache, acne, etc.) and similar to known class effects (7, 8). In the BRAVE-AA studies, patients treated with baricitinib had higher rates of acne and transient creatine kinase and lipid elevations than placebo (7). However, no drug-related deaths or thromboembolic events were reported through 52 weeks. A meta-analysis of nine trials (n = 1,780) found no significant increase in severe adverse events or treatment discontinuations with JAK inhibitors compared with placebo, with a pooled relative risk of 0.77 for both outcomes. However, the overall rate of treatment-related events, mostly minor infections, was modestly higher with JAK inhibitors (pooled relative risk 1.25; 95% confidence interval 1.00–1.57) (12). Long-term extension studies support a stable safety profile; for baricitinib, 104-week data showed maintained efficacy with no new safety signals noted (10). Nonetheless, known risks of JAK inhibitors, such as serious infections, malignancy, and thrombosis, were seen in rheumatoid arthritis patients. Regulatory labels carry warnings about these rare events, although none were uniquely seen in the alopecia trials to date. Importantly, patient monitoring (labs and infection screening) is recommended in clinical use. The newer agents ritlecitinib and deuruxolitinib were approved partly based on favorable tolerability; ritlecitinib's approval (first in adolescents ≥ 12 years; ages 12 to 75 years in trial) reflects its novel selectivity and the absence of unexpected toxicities in its trial (14). No new safety signals specifically attributable to AA patients have emerged in trials, but clinicians should monitor patients closely (16).

Despite their promise, JAK inhibitors have limitations. A substantial fraction of patients do not achieve full regrowth; for example, only about one-third to one-half reach SALT ≤ 20 even on the higher doses, and complete (SALT ≤ 10) responses remain uncommon (7, 9). Crucially, AA is a relapsing disease, and regrowth typically diminishes after drug withdrawal, and so long-term or maintenance therapy may be required. Trial durations have generally been 24 to 52 weeks, and the durability of remission off-treatment is not established. Longer-term safety and optimal treatment duration are still under study (the BRAVE investigators explicitly call for multi-year data) (7). Patient heterogeneity is another challenge; trial participants were mostly adults without significant comorbidities, and so data in children < 12 years, the elderly, or those with severe systemic disease are sparse. Cost and access also affect real-world use of JAK inhibitors. In summary, high-quality evidence shows that oral JAK inhibitors can induce meaningful hair regrowth in moderate-to-severe AA (7, 19). Ongoing research, including head-to-head comparisons, combination strategies, and longer follow-up, will further define the place of JAK therapy in AA (17, 18, 20). Emerging combination approaches, such as JAK inhibitors administered alongside microneedling to enhance follicular penetration or combined with topical sensitizers (e.g., diphencyprone) have shown preliminary efficacy in small studies and may offer synergistic benefits, warranting formal investigation in controlled trials (21) (Table 1).

Table 1 | **Comparison of JAK inhibitors used for the treatment of alopecia areata and those currently in the phase of investigation, and their efficacy, safety profiles, treatment outcomes, and side effects.**

JAK inhibitor	Target	Key trials	Efficacy	Safety profile	Treatment outcome	Side effects
Baricitinib	JAK1/2	Phase 3 RCT	38.8% of patients receiving 4 mg of baricitinib achieved a SALT score ≤ 20 at week 36 (10)	Good tolerability, see above for specific	FDA approved (2022), EMA approved, high patient satisfaction	URTI, nausea, headache, increased cholesterol levels, elevated liver enzymes
Ritlecitinib	JAK3 / TEC family kinase	Phase 2b/3	23% of patients achieved a SALT score ≤ 20 at week 24 and 31% by week 48 (9)	Good tolerability, nasopharyngitis, headache, URTI, and nausea	FDA approved (2023), EMA approved, well suited for younger patients	Nasopharyngitis, headache, acne, diarrhea, fatigue, nausea
Brepocitinib	TYK2 / JAK1	Phase 2 trials completed	SALT score improvement in ~30% (preliminary)	Well tolerated in limited studies	Promising due to dual inhibition of TYK2/JAK1	Acne, upper respiratory infections, headache
Deuruxolitinib	JAK1/2	Phase 3 trials completed	~30% to 41% achieved SALT ≤ 20 at 24 weeks (higher dose)	Well tolerated, dose-dependent adverse effects	Promising alternative to baricitinib with similar response rate	Headache, acne, nasopharyngitis, elevated CPK, liver enzymes
ATI-502 (topical)	JAK1/3	Phase 2 trials completed	Modest regrowth in ~28% (based on investigator global assessment)	Excellent topical safety, minimal systemic absorption	Less effective than oral JAK; low risk makes it suitable for limited patches	Mild irritation at application site
ATI-1777 (topical)	JAK1/3	Phase 2a trials initiated	Early data not yet public	Designed for minimal systemic exposure	Still investigational; could suit patients with localized AA	Local skin effects only
SHR0302	Selective JAK1	Phase 2 trial completed	Moderate efficacy; ~25% to 30% regrowth in responders	Mild; JAK1 selectivity lowers systemic risk	Considered safe and moderately effective in Asian populations	Headache, mild GI symptoms, increased cholesterol levels, thrombocytopenia, raised liver enzymes
Delgocitinib	JAK1/2/3 and TYK2	Topically tested for dermatological diseases and AA early phase	Limited data in AA; effective in eczema	Safe topical use; no serious systemic events	Possibly helpful in scalp application; awaiting AA-specific results	Application site irritation

AA = alopecia areata, CPK = creatine phosphokinase, EMA = European Medical Agency, FDA = food and drug administration, GI = gastrointestinal, JAK = Janus kinase, JAK = Janus kinase inhibitors, RCT = randomly controlled trial, SALT = Severity of Alopecia Tool, TEC = tyrosine kinase, URTI = upper respiratory tract infection, UTI = urinary tract infection, TYK2 = tyrosine kinase 2.

TABLE 25.3
Differences in the Frequency of Adverse Events by Oral JAK Inhibitor

	Very Common (May Affect More Than 1 in 10 Patients)	Common (May Affect up to 1 in 10 Patients)	Uncommon (May Affect up to 1 in 100 Patients)
Abrocitinib	• Nausea	• Abdominal pain • Acne • Dizziness • Headache • Increased CPK • Infections and infestations (herpes simplex, herpes zoster) • Vomiting	• DVT/PE • Hyperlipidaemia (dyslipidaemia, hypercholesterolaemia) • Lymphopenia • Pneumonia • Thrombocytopenia
Baricitinib	• Hypercholesterolaemia • Upper respiratory tract infections	• Abdominal pain • Acne • Headache • Increased ALT • Increased CPK • Infections and infestations (herpes zoster, herpes simplex, gastroenteritis, UTI, pneumonia) • Nausea • Thrombocytosis • Rash	• Diverticulitis • DVT/PE • Facial swelling • Hypertriglyceridemia • Increased AST • Increased weight • Neutropoenia • Urticaria
Upadacitinib	• Acne • Upper respiratory infections	• Abdominal pain • Anaemia • Cough • Fatigue • Headache • Hypercholesterolaemia • Increased AST and ALT • Increased CPK • Increased weight • Infections and infestations (bronchitis, herpes zoster, herpes simplex, folliculitis, influenza) • Neutropoenia • Pyrexia • Urticaria	• Diverticulitis • Hypertriglyceridemia • Oral candidiasis • Pneumonia

Abbreviations: ALT, alanine transaminase; AST, aspartate transaminase; CPK, creatine phosphokinase; DVT, deep vein thrombosis; HDL, high-density lipoprotein; LDL, low density lipoprotein; PE, pulmonary embolism; UTI, urinary tract infection.

- Variation in adverse effects: Adverse events experienced by AD patients receiving treatment with other oral JAK inhibitors are similar to those experienced by patients receiving treatment with baricitinib, although gastrointestinal adverse events such as nausea and vomiting may be especially common in patients receiving abrocitinib. Upadacitinib and abrocitinib preferably inhibit JAK1 while minimally inhibiting JAK2; this theoretically decreases the risk of unwanted haematological adverse events, such as anaemia and neutropenia, as compared to the risk with therapeutic agents with increased inhibition of JAK2.

the likelihood of side effect development, motivational interviewing and cues to action (Tables 4.2 and 4.3). For example, it is important to give sufficient instructions to patients about the use of their systemic and topical therapy, as well as education regarding side effect profiles of the relevant medications. Motivational interviewing successfully resulted in a positive correlation between increased patient education and greater adherence for osteoporotic patients who received a multidisciplinary patient education program [31]. Another study of seven patients treated with adalimumab showed that patient education can be used as a tool to increase adherence [14].

Another method of decreasing patient fear of medication side effects is by putting into practice the old adage of "start low and go slow." Minimizing drug dosage in systemic therapy may necessitate multimodal therapy for optimal treatment results and limitation of side effects [20]. Though adding more medications may minimize dose and side effects, thus increasing treatment efficacy, it may also confuse patients and lead to lower compliance.

Conversely, more aggressive therapy administered for shorter periods of time may be another approach to avoid adverse effects of medications. This theory supports that short-duration, high-potency pharmacotherapy can be better than lower potency medication administered over a longer period of time, and may be ideal for patients who tend to be nonadherent [9]. Aggressive therapy places the focus on decreasing time of intervention and increasing efficacy, providing an alternative to increase patient adherence [9]. Since the patient receiving aggressive therapy may see results more quickly, this may further increase their trust in the medication and their adherence. Ultimately, route of medication administration, severity of disease, patient preference, and lifestyle should all be considered when

Table 4.2 Comparison of biologic medications used to treat psoriasis [30] [data derived from Treatment Comparison. In: treatments BtaTsato, editor. https://wwwpsoriasis.org/sites/default/files/treatment_comparison_chart_1pdf: National Psoriasis Foundation; 2016]

Treatment	Common side effects	Other risks	Monitoring
Certolizumab pegol (Cimzia)	Rash Upper respiratory infection Urinary tract infection	Hepatitis B reactivation Lupus-like syndrome Neurologic symptoms	Complete blood count Hepatic function Tuberculosis (TB) screening
Secukinumab (Cosentyx)	Upper respiratory infection Cold symptoms Diarrhea	Inflammatory bowel disease Reactivation of latent infections	Tuberculosis (TB) screening Hypersensitivity reactions
Etanercept (Enbrel)	Injection-site reaction Upper respiratory infection	Blood dyscrasias Hepatitis B reactivation Lupus-like syndrome Neurologic symptoms New or worsening heart failure	Complete blood count Hepatic function Tuberculosis (TB) screening
Adalimumab (Humira)	Headache Injection-site reaction Upper respiratory infection	Blood dyscrasias Hepatitis B reactivation Lupus-like syndrome Neurologic symptoms New or worsening heart failure	Complete blood count Hepatic function Tuberculosis (TB) screening
Infliximab (Remicade)	Abdominal pain Headache Upper respiratory infection	Blood dyscrasias Hepatitis B reactivation Lupus-like syndrome Neurologic symptoms New or worsening heart failure Lymphoma and other malignancies	Complete blood count Hepatic function Tuberculosis (TB) screening
Golimumab (Simponi)	Injection-site reaction Upper respiratory infection Cold symptoms	Blood dyscrasias Hepatitis B reactivation Lupus-like syndrome Neurologic symptoms New or worsening heart failure Lymphoma and other malignancies	Complete blood count Hepatic function Tuberculosis (TB) screening
Ustekinumab (Stelara)	Fatigue Headache Upper respiratory infection	Reversible posterior leukoencephalopathy syndrome Malignancies	Tuberculosis (TB) screening
Ixekizumab (Taltz)	Fungal infections Injection-site reaction Nausea	Hepatitis B reactivation	Hypersensitivity reactions

Table 17.2 Efficacy of biologic therapies in nail psoriasis

Agent	Dosing	Patients (*n*)	Trial type	Weeks	Outcomes (note different primary outcome measures)	References
Adalimumab	80 mg/40 mg eow	72	RPCDBT in hand/foot psoriasis	16	50% reduction in NAPSI (8% for placebo)	[40]
Etanercept	50 mg biw/50 mg qw	711	Randomized dose comparison	24	82.3% NAPSI 50 response	[42]
Golimumab	100 mg q4 weeks	405	RPCDBT in psoriatic arthritis	24	54% reduction in NAPSI (0% for placebo)	[43]
Infliximab	5 mg/kg weeks 0,2, and 6 then q8 weeks	378	RPCDBT, data from the open-label extension	50	67.8% reduction in NAPSI (49.2% with complete nail clearance)	[45]
Ustekinumab	45 or 90 mg at weeks 0, 4, 16	545	RDBPCT	24	46.5%(45 mg), 48.7%(90 mg) reduction in NAPSI	[48]
Secukinumab	150 or 300 mg at weeks 1–5 then q4 weeks	198	RDBPCT of patients with nail disease, data from the open-label extension	32	52.6% (150 mg) and 63.2% (300 mg) reduction in NAPSI	[52]
Ixekizumab	80 mg q2 or q4 weeks for 12 weeks then 80 mg q4 weeks	1346	RDBPCT, retrospective analysis of open-label period	24	34% and 30% with no nail involvement (NAPSI = 0) on q2 and q4 doses, respectively	[51]

Legend: *eow* every other week, *NAPSI* nail area psoriasis severity index, *RDBPCT* randomized double-blind placebo-controlled trial

of patients with psoriasis involving the hands and/or feet, demonstrated 50% improvement in NAPSI at 16 weeks compared with 8% for placebo [40]. In a study evaluating both fingernails and toenails, open-label adalimumab showed improvements at 6 months in NAPSI of 85% and 72% in fingernails and toenails, respectively [41]. An open-label study of etanercept in nail psoriasis compared patients randomized to two dosing regimens: 50 mg twice weekly for 12 weeks followed by 50 mg weekly for 12 weeks, or 50 mg weekly for 24 weeks. A 50% improvement in NAPSI was demonstrated in 58.1% and 82.3% of patients in the twice-weekly/weekly group and 50.5% and 80.7% in the weekly group at 12 and 24 weeks, respectively [42]. In a RDBPCT patients with psoriatic arthritis were treated with placebo, golimumab 50 mg every 4 weeks, or golimumab 100 mg every 4 weeks for 24 weeks. Median percent change in NAPSI at weeks 14 and 24 was 0%, 25%, and 43% and 0%, 33%, and 54% for the placebo, golimumab 50 mg, and golimumab 100 mg groups, respectively. Patients in this trial for psoriatic arthritis were allowed to use stable doses of methotrexate and prednisone during the study [43]. Currently golimumab is FDA approved for psoriatic arthritis but not for psoriasis. In a RDBPCT of infliximab, patients were randomized to either placebo or infliximab 5 mg/kg at weeks 0, 2, 6, and every 8 weeks through week 46, with placebo crossover at week 24. Mean percentage improvement in target nail NAPSI at weeks 10 and 24 was 26.8% and 57.2%, compared with −7.7% and −4.1% for infliximab and placebo, respectively [44]. In a retrospective analysis of patients from this same infliximab study, mean NAPSI improvement was 28.3%, 61.4%, and 67.8%, at weeks 10, 24, and 50, respectively [45].

No controlled comparisons of anti-TNF agents in nail psoriasis have been performed. However, an open-label prospective study showed that infliximab was superior to adalimumab and etanercept at 14 weeks [46]. A retrospective comparison of these agents also showed high efficacy of all the TNF-blocking agents in nail psoriasis with some greater improvement with infliximab [47]. The differences in efficacy of these agents in nail psoriasis may parallel the differences seen in skin response. Infliximab may also have an advantage in the speed to which clearance is achieved. However, after 4 months or more, all anti-TNF therapies are successful in improving nail disease by at least 50%, as measured by NAPSI.

Robust data is also available for IL-12/23 blockade in nail psoriasis. Data from a large phase III trial of ustekinumab showed significant improvement in NAPSI compared with placebo at 12 weeks. Additionally, the ustekinumab 45 mg and 90 mg groups showed 46.5% and 48.7% NAPSI improvement, respectively, at 24 weeks [48]. Long-term data with 68 weeks of ustekinumab in a Japanese study showed a

- The dramatic effectiveness of cyclosporine was the first hard clue pointing to the central role of T cells in psoriasis and triggering the many investigative efforts that made possible the host of biological agents that are now available.
- The long-term side effects of cyclosporine are too great to make it a routine drug for psoriasis.

► **Biologicals:** These are therapeutic molecules that are specifically targeted in order to imitate or inhibit naturally occurring proteins. The main categories currently used are antibodies and fusion proteins, which either antagonize mediators with a central pro-inflammatory role or interfere with the interactions between T cells and endothelial cells or antigen-presenting cells (APC). Table 16.**5** summarizes the biologicals available in Europe for the treatment of psoriasis. The fascinating scientific background, targeting, efficacy, and relative paucity of side

Table 16.4 · **Biological agents for psoriasis and psoriatic arthritis**

Indications	Dose	75% PASI ↓	Joint response	Side effects
Alefacept				
Moderate to severe psoriasis	7.5 mg i. m. weekly	35% after 14 weeks	55%	↘CD4+ T cells Autoantibodies (2%)
Efalizumab				
Moderate to severe psoriasis	1 mg/kg subq. weekly	36% after 12 weeks	None	Guttate flares during initial treatment; risk of rebound when treatment stopped
Etanercept				
Psoriatic arthritis, rheumatoid arthritis	25–50 mg subq. 2× weekly	35% after 12 weeks	60–70%	Delayed hypersensitivity reaction at injection site Anti ds-DNA antibodies Infections (long-term therapy)
Infliximab				
Psoriatic arthritis, rheumatoid arthritis, Crohn disease, others	5 mg/kg i. v. at weeks 0, 2, and 6	> 80% after 10 weeks	~70%	Infusion reactions Autoantibodies (10%) Infections (tuberculosis) Anaphylaxis (< 0.1%)

Sterry, Dermatology © 2006 Thieme
All rights reserved. Usage subject to terms and conditions of license.

INDICATIONS AND CONTRAINDICATIONS FOR COMMERCIALLY AVAILABLE TARGETED IMMUNE MODULATORS ('BIOLOGIC' AGENTS)
Indications
General Indications
• Patients with moderate to severe psoriasis, eligible for a systemic treatment • Patients with psoriatic arthritis, particularly those who have failed to improve with other disease-modifying antirheumatic drugs (DMARDs)
Restricted Indication
• Patients with moderate to severe psoriasis who are not candidates for topical treatments, phototherapy, or classic systemic treatments because of insufficient efficacy or contraindications
Contraindications
(The exact contraindications vary by agent; some listed below are relative, while others are absolute [*]) • Significant viral, bacterial, or fungal infections* • Increased risk for developing sepsis* • Active tuberculosis* • Immunosuppressed patient • Past history of hepatitis B • Pregnancy (TNF-α inhibitors, alefacept† and ustekinumab are category B) • Breast-feeding • Malignancy within the past 5 years (does not include adequately treated cutaneous squamous or basal cell carcinoma) • Excessive chronic sun exposure or phototherapy • Allergic reaction to the biologic agent* • Selective for alefacept†: CD4 counts <250 cells/mcl*; HIV infection* • Selective for TNF-α inhibitors: ANA+ (especially if high titer) or autoimmune connective tissue disease, lymphoma, congestive heart failure (NYHA grade III or IV), or demyelinization disorders (the latter also in first-degree relatives)* • Selective for ustekinumab: BCG vaccination within the past 12 months (mode of action expected to increase susceptibility to mycobacterial infections)
†Production of alefacept in the United States was discontinued in 2011. *BCG, bacillus Calmette–Guérin; NYHA, New York Heart Association.*

Table 6.7 Indications and contraindications for commercially available targeted immune modulators ('biologic' agents). Administration of live vaccines is contraindicated in patients receiving biologic agents for psoriasis. *Courtesy, Peter C. M. van de Kerkhof, MD.*

TREATMENT OF THE PSORIATIC PATIENT WITH COMORBIDITIES OR SPECIAL SITUATIONS	
Comorbidity or Special Situation	**Potential Treatment(s)**
History of internal malignancy (e.g. lymphoma and lung cancer)	Topical agents UVB phototherapy Oral retinoids
Liver disease	Topical agents UVB phototherapy Targeted immunomodulators ('biologic' agents) (e.g. etanercept)
Hepatitis B* or C viral infection	Etanercept > adalimumab, ustekinumab

Table 6.8 Treatment of the psoriatic patient with comorbidities or special situations. Targeted immunomodulators ('biologic' agents) are contraindicated in patients with active tuberculosis. *Continued*

Table 6.8 *Continued* **Treatment of the psoriatic patient with comorbidities or special situations.** Targeted immunomodulators ('biologic' agents) are contraindicated in patients with active tuberculosis.

Comorbidity or Special Situation	Potential Treatment(s)
Metabolic syndrome	Topical agents Phototherapy Methotrexate† Oral retinoids† Targeted immunomodulators ('biologic' agents)
Pregnancy	Topical CS (limited use of mild- to moderate-strength CS) UVB phototherapy Targeted immunomodulators ('biologic' agents) (anti-TNF agents and ustekinumab are category B) Cyclosporine (category C)
Immunosuppression (e.g. HIV infection/AIDS)	Topical agents UVB phototherapy Oral retinoids
Numerous skin cancers	Topical agents Oral retinoids

**In hepatitis B surface antigen (HBsAg) carriers, either anti-HBV treatment or prophylaxis is required to prevent hepatitis reactivation; others require careful monitoring.*
†Caution with use in patients with fatty liver.

RECOMMENDED LABORATORY EVALUATION FOR PATIENTS RECEIVING TARGETED IMMUNOMODULATORS FOR PSORIASIS

Drug	Prior to treatment	During treatment
TNF-α inhibitors (e.g. adalimumab, etanercept, infliximab) or ustekinumab	Tuberculin skin test*/interferon-γ release assay** and/or (e.g. if immunosuppression or history of tuberculosis) chest x-ray CBC, CMP Hepatitis B and C virus serologic profiles Consider HIV testing	Annual tuberculin skin test*/interferon-γ release assay** and/or chest x-ray CBC or CMP every 3-12 months (or as clinically indicated)

**≥5 mm of induration should be considered as positive.*
***e.g. QuantiFERON® TB Gold or T-SPOT®.TB.*
CMP, comprehensive metabolic panel (includes liver function tests); PPD, purified protein derivative.

Table 6.9 Recommended laboratory evaluation for patients receiving targeted immunomodulators for psoriasis. A complete medical history and physical examination should also be performed, with particular attention to history/risk/symptoms/signs of tuberculosis, other chronic infections, malignancy, neurologic disorders and cardiac disease (especially congestive heart failure in patients receiving TNF-α inhibitors).

For further information see Ch. 8. From *Dermatology, Third Edition*.

TABLE 28-7

Biologic Treatments for Psoriasis

	USTEKINUMAB	ETANERCEPT	INFLIXIMAB	ADALIMUMAB	SECUKINUMAB	IXEKIZUMAB
Mechanism	Binds p40 (the common subunit of IL-12 and IL-23); blocks Th1 and Th17 differentiation and proliferation	Human recombinant, soluble TNF-α receptor; binds TNF-α and neutralizes its activity	Chimeric monoclonal antibody that has high specificity, affinity, and avidity for TNF-α	Fully human recombinant monoclonal antibody that specifically targets TNF-α	Fully human recombinant monoclonal antibody that specifically targets IL-17A	Humanized monoclonal antibody that specifically targets IL-17A
Dosing	SC injections; weight-based dosing Individuals weighing <100 kg (220 lb): 45 mg Individuals weighing >100 kg: 90 mg Injections at wk 0 and 4 and then every 12 wk	25- to 50-mg injections SC twice weekly; commonly given as 50 mg twice weekly for 12 wk followed by 50 mg weekly For pediatric patients, recommended dosing is 0.8 mg/kg weekly with a maximum of 50 mg per week	IV infusions over 2 hr; 5–10 mg/kg at weeks 0, 2, and 6	Initial dose of 80 mg followed by 40 mg given every other week starting 1 week after the initial dose	150- to 300-mg injections at weeks 0, 1, 2, 3, and 4 (loading dose) followed by injections every 4 wk	160-mg injection at week 0 followed by 80 mg at weeks 2, 4, 6, 8, 10, and 12; then 80 mg every 4 wk
Efficacy	PASI-75 at 12 wk, 67%; 71%–78% at wk 28	PASI-75 at 12 wk, 34% and at 24 wk, 44% for the 25-mg twice-weekly vs 49% and 59% for 50-mg twice-weekly dosing	PASI-75 at 10 wk, 82% (5 mg/kg) and 91% (10 mg/kg); at wk 26 (after a single course), 57% of patients maintained PASI-50, and 50% maintained PASI-75	PASI-75 at 16 wk, 71%	PASI-75 at week 12 in the range of 77%–82% PASI-90 52%–59% and PASI-100 24%–29% for 300-mg dosing	PASI-75 at week 12 achieved in 87% of patients; PASI-90 in 68% and PASI-100 in 38% of patients
Safety	Serious infections, increased risk of malignancy, reversible posterior leukoencephalopathy syndrome; live vaccinations not recommended	Serious infections, exacerbation of MS, pancytopenia, malignancy, worsening congestive heart failure; lupus-like symptoms (anti-dsDNA positive); live vaccinations should not be given	Infusion-related reactions, infections, worsening of MS, malignancy, or lymphoproliferative disease, worsening heart failure; lupus-like symptoms (anti-dsDNA positive); live vaccinations should not be given	Injection site reactions, infections, lupus-like syndrome, worsening heart failure, cytopenias, neurologic events; live vaccinations should not be given	Infections, particularly nasopharyngitis; exacerbation of IBD; hypersensitivity reactions; patients should not receive live vaccines while on treatment	Infections; hypersensitivity reactions; exacerbation of IBD
Monitoring	Baseline PPD/QuantiFERON-TB Gold	Baseline PPD/QuantiFERON-TB Gold	Baseline PPD/QuantiFERON-TB Gold	Baseline PPD/QuantiFERON-TB Gold	Baseline PPD/QuantiFERON-TB Gold	Baseline PPD/QuantiFERON-TB Gold
Long-term administration	Clinical trials have established safety up to 76wk; appears to be similar to TNF-α inhibitors	PASI response continues to increase to wk 24; large databases in patients with other immunologic diseases indicate safety	As intermittent therapy; large databases in patients with other immunologic diseases indicate relative safety	Similar to other TNF-α inhibitors	Clinical trials have shown maintenance of efficacy beyond 52 wk of treatment	Clinical trials have shown maintenance of efficacy beyond 60 wk of treatment
Pregnancy Category	B	B	B	B	B	B

dsDNA, double-stranded DNA; IBD, inflammatory bowel disease; IL, interleukin; IV, intravenous; LFA, lymphocyte function–associated antigen; MS, multiple sclerosis; PASI-50, 50% improvement in Psoriasis Area and Severity Index; PASI-75, 75% improvement in Psoriasis Area and Severity Index; PPD, purified protein derivative (of tuberculin); SC, subcutaneous; TNF, tumor necrosis factor.

TABLE 18-6
Biologic Treatments for Psoriasis

	ALEFACEPT	EFALIZUMAB	ETANERCEPT	INFLIXIMAB	ADALIMUMAB
Mechanism	Binds CD2 on T cells, blocking the CD2-LFA3 interaction, thus interfering with T-cell activation and causing T-cell apoptosis.	Binds CD11a (α subunit of LFA-1). Blocks the interaction of LFA-1 with intercellular adhesion molecule-1. Inhibits T-cell activation, trafficking, and adhesion to keratinocytes.	Human recombinant, soluble TNF-α receptor. Binds TNF-α and neutralizes its activity.	Chimeric monoclonal antibody that has high specificity, affinity, and avidity for TNF-α.	Fully human recombinant monoclonal antibody that specifically targets TNF-α.
Dosing	15 mg IM once weekly.	Subcutaneous injections. Conditioning: 0.7 mg/kg. Maintenance: 1 mg/kg weekly.	25- to 50-mg injections subcutaneously twice weekly.	Intravenous infusions over 2 h. 5–10 mg/kg at weeks 0, 2, and 6.	40-mg injections subcutaneously every other week.
Efficacy	PASI-75 at 14 wk (2 wk after last dose) 24%. Patients who respond maintain improvement for extended periods of time. Repeat courses are safe and well tolerated.[385]	PASI-75 at 12 wk, 22%–41%;[386–388] at 24 wk, 44%;[389] and at 27 mo of extended treatment, 56%.[388]	PASI-75 at 12 wk, 34% and at 24 wk, 44%.[390]	PASI-75 at 10 wk, 82% (5 mg/kg) and 91% (10 mg/kg).[391] At wk 26 (following a single course), 57% of patients maintained PASI-50, and 50% maintained PASI-75.[391]	PASI-75 at 24 weeks 59%.[392]
Safety	Lymphopenia, malignancy, serious infections. Not recommended for human immunodeficiency virus–positive patients. Effects of live vaccines not studied.	Serious infections, thrombocytopenia, exacerbation of psoriasis. Live vaccinations not recommended.	Serious infections, exacerbation of MS, pancytopenia, malignancy. Worsening congestive heart failure. Lupus-like symptoms (anti-dsDNA positive). Live vaccinations should not be given.	Infusion-related reactions, infections, worsening of MS, malignancy or lymphoproliferative disease, worsening heart failure. Lupus-like symptoms (anti-dsDNA positive). Live vaccinations should not be given.	Injection site reactions, infections, lupus-like syndrome, worsening heart failure, cytopenias, neurologic events.[393] Live vaccinations should not be given.
Monitoring	$CD4^+$ T-cell counts every 2 wk during treatment.	Regular platelet counts.	Baseline PPD.	Baseline PPD.	Baseline PPD.
Long-term administration	Up to nine courses have been administered over 4–5 yr in small number of patients with incremental benefits.	PASI responses continue to increase to wk 24 and are maintained in patients receiving long-term continuous therapy (up to 24 mo).	PASI response continues to increase to wk 24. Large databases in patients with other immunologic diseases indicate safety.	As intermittent therapy. Large databases in patients with other immunologic diseases indicate relative safety.	Expected to be similar to other TNF-α inhibitors.
Pregnancy category	B	C	B	B	B

dsDNA = double-stranded DNA; LFA = lymphocyte function–associated antigen; MS = multiple sclerosis; PASI-50 = 50% improvement in Psoriasis Area and Severity Index; PASI-75 = 75% improvement in Psoriasis Area and Severity Index; PPD = purified protein derivative (of tuberculin); TNF = tumor necrosis factor.

lished phenomenon in psoriasis.[261] Long-term topical corticosteroids may cause striae (Fig. 18-17) and adrenal suppression. This class of agents is discussed in detail in Chap. 225.

VITAMIN D_3 AND ANALOGUES[262] Vitamin D exerts its actions by binding to the vitamin D receptor, another member of the nuclear hormone receptor superfamily. Vitamin D_3 acts to regulate cell growth, differentiation, and immune function, as well as calcium and phosphorous metabolism. Vitamin D has been shown to inhibit the proliferation of keratinocytes in culture and to modulate epidermal differentiation. Furthermore, vitamin D inhibits production of several pro-inflammatory cytokines by psoriatic T-cell clones, including IL-2 and IFN-γ.[263]

Analogues of vitamin D that have been used for the treatment of skin diseases are calcipotriene, (calcipotriol), tacalcitol, and maxacalcitol. In short-term studies, potent topical corticosteroids were found to be superior to calcipotriene. When compared with short-contact anthralin or 15 percent coal tar, calcipotriene was the more effective agent. The efficacy of calcipotriene is not reduced with long-term treatment.[264] Calcipotriene applied twice daily is more effective than once-daily use. Hypercalcemia is the only major concern with the use of topical vitamin D preparations. When the amount used does not exceed the recommended 100 g/week, calcipotriene can be used with a great margin of safety.[265] Vitamin D analogues are often used in combination with or in rotation with topical corticosteroids in an effort to maximize therapeutic effectiveness while minimizing steroid-related skin atrophy.

ANTHRALIN (DITHRANOL) Dithranol (1,8-dihydroxy-9-anthrone) is a naturally oc-

Table 81.1 Therapies for psoriasis

	Recommended dose	Remarks
Topical therapies		
Corticosteroids	Once daily	Limited period of 2–4 weeks
	No more than 50 g/week	
Vitamin D3 derivatives	Tacalcitol once daily, calcipotriol twice daily	Their use can be longer than corticosteroids (alone or in combination)
Combined therapy with vitamin D3 derivatives and corticosteroids	Once daily	Limited period of 2–4 weeks
Retinoids	Once daily	Possibility of short-contact therapy
Topical calcineurin inhibitors	Once daily	As maintenance therapy for intertriginous areas
Phototherapy and laser therapy	UVA1: medium (40–80 J/cm^2) and high (80–120 J/cm^2) doses	UVB broad- and narrowband phototherapy
	NB-UVB initial dose (75–100 % minimal erythema dose) to be increased	UVB 308–311 laser therapy
		UVA1 phototherapy
		UVA1 355 nm laser therapy
PUVA	8-methoxypsoralen (8-MOP) 0.3–0.6 mg/kg 1–2 h prior UVA exposure (1 J/cm^2), then increasing UVA doses	
Systemic therapies		
Cyclosporine	2.5–5 mg/kg/die (optimal 4 mg/kg/die)	The average duration of treatment between 8 and 16 weeks and median time to relapse is about 72 days
Methotrexate	5–10 mg weekly as initial dose, escalation dose up to 30 mg weekly	Two dosage schedules (single weekly or intermittent oral schedule (Weinstein regimen))
Acitretin	0.3–0.8 mg/kg/die (optimal 0.5 mg/kg/die)	Useful in pustular and acral psoriasis
Fumaric acid esters	Up to 1.2 g daily	
Adalimumab	80 mg at week 0, 40 mg at week 1, then 40 mg every 2 weeks	
Etanercept	50 mg biweekly for plaque psoriasis for 12 weeks, then 50 mg weekly	
	50 mg weekly for psoriatic arthritis	
Infliximab	5 mg/kg at weeks 0, 2, and 6 and every 8 weeks	
Golimumab	50 mg if body weight <100 kg, 100 mg if body weight >100 kg every 4 weeks	
Ustekinumab	45 mg if body weight <100 kg, 90 mg if body weight >100 kg at week 0, at week 4, and every 12 weeks	

Recommended doses for both topical and systemic therapies

antiproliferative and anti-inflammatory effects and is a useful drug in rheumatoid arthritis, systemic lupus erythematosus, dermatomyositis, sarcoidosis, immunobullous disorders, and psoriasis. MTX has an antiproliferative effect as a folic acid antagonist on the basis of its competitive binding to dihydrofolate reductase. Despite these well-known pharmacological effects, the mechanism of action of MTX at low dose in the treatment of psoriasis remains unclear, having both *immunomodulatory* and profound *anti-inflammatory* properties.

Table 81.2 Common potential adverse events related to the use of systemic conventional therapies and biologics

Agents	Potential occurrence of important side effects				
	Very frequent	Frequent	Occasional	Rare	Very rare
Infliximab	Infusion reactions	Infections, headache, flush, pruritus, urticaria, fever, transaminase elevation	Serum-sickness-like disease, (cutaneous) lupus erythematodes syndrome, severe infections, tuberculosis, anaphylactoid reaction	Opportunistic infections, pancytopenia, vasculitis, demyelinating diseases	
Etanercept	Injection-site reactions, infections (upper respiratory tract, bronchitis, skin infections)	Pruritus	Thrombocytopenia, urticaria, angio-oedema, severe infections (pneumonia, cellulitis, sepsis), weight gain	Anaemia, leucopenia, neutropenia, pancytopenia, vasculitis, subacute and discoid lupus erythematodes, demyelinating disease, tuberculosis	Aplastic anaemia
Adalimumab	Injection-site reaction	Upper respiratory tract infections, sinusitis, injection-site reactions, headache, and rash	Tuberculosis		Drug-induced lupus, lymphoma
Golimumab	Upper respiratory tract infection, viral infections, bronchitis, superficial fungal infections, sinusitis, injection-site reaction	Hypertension, dizziness, paresthesia, constipation, liver enzyme elevations		Vasculitis, other infections and infestations	
Ustekinumab	Upper respiratory infections, headache, tiredness, injection-site reaction, back pain, fatigue	Itching, joint pain, muscle pain or tenderness, injection-site reaction, skin rash or rashes, sore throat, urticaria, depression, diarrhoea, hypersensitivity reaction, dizziness	Other infections	Facial palsy	

(continued)

Table 81.3 Screening tests required for systemic drug prescription

Agent	Full blood count	Liver enzymes	Serum creatinine	Urine sediment	Pregnancy test (urine)	HBV/ HCV	Serum albumin	PIIINP where available	Electrolytes	Uric acid	Cholesterol, triglycerides	Magnesium	Fasting blood sugar	ESR, CRP	HIV	TB gold quanti-feron
MTX	X	X	X	X	X	X	X	X			X					
Cya	X	X	X	X	X				X	X	X	X				
Retinoids	X	X	X		X						X		X			
FAEs	X	X	X	X	X						X					
Adalimumab	X	X	X	X	X	X					X			X	X	X
Etanercept	x	X	X	X	X	X					X			X	X	X
Infliximab	X	X	X	X	X	X					X			X	X	X
Ustekinumab	X	X	X	X	X	X					X			X	X	X
Golimumab	X	X	X	X	X	X					X			X	X	X

Psoriasis – Biologics (Dosing)

Table 92 Biologics commonly used in the treatment of psoriasis

Generic name	Trade name	Treatment regimen	Monitoring	Comments
Alefacept	Amevive	15 mg IM q week × 12 weeks	CD4 at baseline and q 2 weeks	May repeat course 12 weeks after end of last course in normal $CD4^+$
Etanercept	Enbrel	(1) 50 mg SC 2x/week × 3 months, then decrease to maintain dose of 50 mg SC weekly (2) 50 mg SC 2x/week × 3 months, then 25 mg SC 2x/week	PPD at baseline	Psoriatic arthritis dosing is 25 mg SC 2x/week
Adalimumab	Humira	40 mg SC q 2 week	PPD at baseline	**Black box warning** re: TB, invasive fungal infections, opportunistic infections
Efalizumab	Raptiva	Start 0.7 mg/kg SC (max 200 mg/dose) × 1, then 1 mg/kg SC q week	Monitor plts q months initially, then q 3 months	The only biologic that is weight-based. May potentially cause flare in arthritic symptoms. **(Removed from US market in April 2009 for increased risk of PML)**
Infliximab	Remicade	Start 5 mg/kg IV × 1 on weeks 0, 2, 6 then 5 mg/kg IV q 8 weeks	PPD at baseline	Psoriatic arthritis dosing is the same **Black box warning** re: TB, invasive fungal infections, opportunistic infections
Ustekinumab	Stelara	<100 kg 45 mg SC at week 0, week 4, q 12 weeks >100 kg 90 mg SC at week 0, week 4, q 12 weeks	PPD at baseline	Approved for psoriasis, but not for psoriatic arthritis
Workup prior to starting biologic: 1) History of CHF? 2) History of multiple sclerosis? 3) History of any malignancy (except NMSC)? 4) Family history of multiple sclerosis? 5) History of tuberculosis? 6) History of chronic infections? 7) History of IV Antibiotics in past year? 8) History of hepatitis? 9) PPD +/− Chest x-ray 10) CBC + diff, LFTs, CMP 11) Document body surface area (BSA)			Rule of Nines(Body surface area): **Arm + Hand (each) ------- 9%** **Leg + Foot (each) --------- 18%** **Front Torso ---------- 18%** **Back Torso + Buttocks --- 18%** **Head + Neck ---------- 9%** **Genital Area (perineum) – 1%**	

Table 42 Biologics used in psoriasis

	Alefacept (Amevive®)	Etanercept (Enbrel®)	Infliximab (Remicade®)	Adalimumab (Humira®)	Ustekinumab (Stelara®)
Description	Fusion protein of human LFA-3 and the Fc portion of IgG1	Fusion protein of the Fc of human IgG1 and the extracellular TNF receptor	Chimeric antibody against TNFα composed of a human IgG1 constant domain and murine variable regions	Recombinant human IgG1 monoclonal antibody against TNFα	Monoclonal antibody (fully human)
Mechanism	Inhibits T-cell activation and proliferation by blocking LFA-3/CD2 interaction, resulting in selective apoptosis of T-cells	Binds soluble TNF and blocks its interaction with cell surface receptors	Binds soluble and bound TNFα	Binds TNF and blocks its interaction with cell surface TNF receptors	Target the p40 subunit of interleukin (IL)-12 and IL-23 which are related to the differentiation of naïve T-cells into Th1 and Th17 cells
FDA indication	Moderate-to-severe plaque psoriasis in adults	Moderate-to-severe plaque psoriasis in adults; psoriatic, rheumatoid, and juvenile RA; ankylosing spondylitits	Severe recalcitrant psoriasis, Crohn's disease, RA	Moderate-to-severe RA in adults	Moderate-to-severe plaque psoriasis in adults
Dosing	15 mg IM q week × 12 weeks, wait 12 weeks, then consider a second course × 12 weeks	50 mg SC BIW × 12 weeks, then 50 mg SC q week	3 mg/kg IV over 2 h at weeks 0, 2, 6, then 5 mg/kg q 8 weeks (preferred psoriasis dose)	40 mg SC over 3–5 min q2 weeks × 12 weeks; can ↑ to q week doses if not on methotrexate	<100 kg 45 mg SC at week 0, week 4, q 12 weeks >100 kg 90 mg SC at week 0, week 4, q 12 weeks
FDA monitoring	CD4 at baseline and weekly (hold dose if < 250 cells/μL)	Screen for latent TB (PPD and/or CXR) at baseline	Screen for latent TB (PPD and/or CXR) at baseline	Screen for latent TB (PPD and/or CXR), routine CBC/chemistries at baseline; anti-dsDNA Ab if lupus-like sx present	Screen for latent TB (PPD and/or CXR) at baseline

Pregnancy and nursing	Preg Cat B, lactation safety unknown	Preg Cat B, lactation safety ? (secreted in breast milk)	Preg Cat B, lactation safety unknown	Preg Cat B, lactation safety unknown	Preg Cat B, lactation safety unknown
Optional monitoring	PPD and/or CXR, and β-HCG at baseline	PPD and/or CXR, BUN, Cr, SGOT, SGPT, Hep C serology and/or β-HCG at baseline Consider periodic CBC, ESR, and clinical follow-up q 3 months	BUN, Cr, SGOT, SGPT, Hep C serology and/or β-HCG at baseline. Consider periodic CBC and clinical follow-up q 3 months	PPD and/or CXR and β-HCG at baseline	PPD and/or CXR, and β-HCG at baseline
Side effects, common	Cough, dizziness, nausea, pharyngitis, pruritus, myalgias, chills, injection site reaction, transaminitis	Injection site reactions (37%), cough and resp sx (45%), infections (35%), headaches (17%), positive ANA (11%)	Nausea, abdominal pain, back pain, arthralgia, fatigue, headache	Injection site reaction (8%), positive ANA (12%)	Nasopharyngitis, URI, headache, fatigue, diarrhea, back pain, dizziness, pruritus, injection site reaction
Side effects, serious	Lymphopenia, malignancies, serious infections, hypersensitivity, transaminase elevations (rare), cardiovascular events	Allergic rxns (<2%), leukopenia, pancytopenia, new onset or exacerbation of CNS demyelinating d/o(rare), ↑ incidence of lymphoma, infections	Hypersensitivity rxn, infusion rxn, exacerb of CHF, infections (same as placebo), TB, invasive fungal infections, lupus-like syndrome	Hypersensitivity rxn, confusion, MS, paresthesia, subdural hematoma, tremor, infections, sepsis, malignancy, TB	Infection, malignancy, reversible posterior leukoencephalopathy syndrome
Contraindications	Hypersensitivity to alefacept, dc if CD4 < 250 × 1 month	Hypersens to etanercept or components, active infections or sepsis. No live vaccines. CHF, poorly controlled diabetes, or immunosupp	Hypersens to infliximab or murine products, CHF (NYHA Class III/IV)	Hypersens to adalimumab, chronic or recurrent infections, latent TB, immunosupp. Avoid concomitant tx with anakinra and TNF-blocking agents	Hypersensitivity to ustekinumab Acute infection, caution if latent tuberculosis, caution if chronic/recurrent infections

(continued)

Table 42 (continued)

	Alefacept (Amevive®)	Etanercept (Enbrel®)	Infliximab (Remicade®)	Adalimumab (Humira®)	Ustekinumab (Stelara®)
Precautions	Infection, history of malignancy, live vaccines	Concurrent tx with anakinra, natalizumab, TNF-blockers or use in patients with preg, renal dz, asthma, CNS demyelin dz or blood dyscrasias	High risk of infection, those with preexisting or recent onset of CNS demyelin dz or seizure d/o, or who have received live vaccines	Mild CHF (NYHA Class I/II) – close cardiac monitoring. DC if lupus-like rash develops. Caution in elderly, patients with preexisting or recent onset of CNS demyelin dz	Infection, history of malignancy
Manufacturer	Astellas	Amgen, Wyeth Pharmaceuticals	Centocor	Abbott	Centocor
Other	* Can use with phototherapy * Max reduction in psoriasis at 8 weeks after last dose * 16-week cycles are under investigation	* Can use with methotrexate	* Can use with MTX * Improvement after first few weeks	* Can use with MTX, steroids, salicylates, NSAIDs	
Relative efficacy	**PASI 75**: 21% at week 14 (2 weeks post dosing) **PASI 50**: 42% at week 14 PASI 50 began 60 days after start Most maintain PASI 50 through 3 months observation period	**PASI 75:** 47% at 3 months, 54% at 6 months **PASI 50:** 71% at 3 months Median time to PASI 50 and 75 was 1 and 2 months, respectively, after start	**PASI 75:** 82% at week 10 and 33% at week 26 (5 mg/kg) **PASI 50:** 40% at week 26 (on 5 mg/kg) Statistically significant reduction in PASI w/respect to placebo 2 weeks after start	**PASI 75:** achieved by week 20 in one out of two patients (maintained though week 40) **PASI 50:** achieved by week 12 and week 16 in 2 out of 2 patients	**PASI 75 (week 12):** 67% with 45 mg dose, 78% with 90 mg

Table 30.7: Combination therapy[578]

Combinations	Comments
Systemic and topical agents:	
PUVA + topical steroids	Rapid clearing, smaller total UVA dose but higher relapse rate
Methotrexate + topical steroid	Beneficial during maintenance therapy
Retinoids + topical steroids	Lower dose of retinoids can be used
UVB + topical steroids	No added efficacy
Cyclosporine + topical steroid, calcipotriol or anthralin	Allows low dosage of cyclosporine, and irritant topical agents can be used because of inflammation is suppressed by cyclosporine
PUVA + topical calcipotriol	Rapid clearing and reduced total UVA dose
UVB + topical tazarotene[579]	Faster clearance than UVB therapy alone
Systemic agents:	
PUVA+ retinoid (Re-PUVA)	Number of PUVA treatments reduced by 50%; retinoid should be started 1–2 weeks earlier
UVB + retinoids	Clearance is achieved with a lower dosage of UVB
PUVA + UVB	Number of PUVA treatments reduced by 30%
PUVA + cyclosporine	As effective as Re-PUVA, however overall exposure to UVA is much higher
UVB + methotrexate	Effective in clearing psoriasis but generally ineffective in maintaining the clearance
PUVA + methotrexate	Though total UVA exposure is reduced by half, the combination increases the risk of skin cancer and methotrexate induced phototoxicity
Methotrexate + cyclosporine	Combination generally not recommended because they inhibit each other's excretion. Can be used with precautions in patients with associated psoriatic arthritis
Cyclosporine + retinoids	Variable efficacy
Methotrexate + retinoids	Used with caution because of potential hepatotoxicity
Methotrexate + sulfasalazine	Used with caution because of potential hepatotoxicity
Sulfasalazine + PUVA	Not recommended because of sulfasalazine induced phototoxicity
Combination therapy with biologicals	
Etanercept + methotrexate[580]	Effective in recalcitrant psoriasis with no additional side effects. Also effective in arthritis
Etanercept + acitretin[580]	Effective in recalcitrant psoriasis with no additional side effects
Etanercept + cyclosporine[580]	Effective in recalcitrant psoriasis with no additional side effects. Also effective in arthritis
Etanercept + calcipotriene ointment[580]	Effective in recalcitrant psoriasis with no additional side effects. Also effective in arthritis
Alefacept + UVB[581,582]	More rapid onset of action with no additional toxicity compared with alefacept monotherapy
Alefacept + immunosuppressants (methotrexate, cyclosporine, etanercept, leflunomide, mycophenolate mofetil and infliximab)[581,582]	No altered frequency and spectrum of adverse events or serious infections with concomitant or prior use of immunosuppressants

Note: PUVA = Psoralen ultraviolet A, Re-PUVA = retinoid-PUVA, UVB = Ultraviolet B.

Table 30.8: Rotational therapy[578]

Rotational drugs	Comments
Methotrexate to PUVA	PUVA is the better alternative and it should not be given on the days of methotrexate therapy to avoid phototoxicity. Methotrexate is withdrawn when the effect of PUVA becomes evident
Methotrexate to cyclosporine	Abnormal liver function induced by methotrexate will not be affected by cyclosporine. However, rotation should be done carefully
Methotrexate to retinoids	Retinoids do not produce chronic liver disease so rotation can be done. Retinoids should be started 2–3 months before stopping primary drug
Retinoids to other agents	Retinoids can be stopped abruptly without producing rebound
Cyclosporine to methotrexate	Careful monitoring of renal function is required during rotation. If renal function does not return to normal, stop methotrexate and start alternative drug
Cyclosporine to phototherapy/re-PUVA	There is a concern for increased risk of skin cancer during phototherapy because of immunosuppression induced by prior cyclosporine
Rotation with hydroxyurea	Rotation to hydroxyurea is beneficial when patient develops severe toxicity or therapeutic plateau with other drugs. When hydroxyurea is used the primary drug can be stopped abruptly without the risk of rebound. Hydroxyurea should not be used just before or after methotrexate because of increased risk of bone marrow suppression

Cost of Psoriasis and Psoriatic Arthritis Therapies

Biologic therapies generally offer good efficacy and safety and have revolutionized the treatment of psoriasis and PsA. However, this comes at a significant financial cost, with the average wholesale price of most biologic therapies reaching tens of thousands of dollars per year. By contrast, MTX is relatively inexpensive, costing only a few dollars per week. To help adjust cost for efficacy, a recent study examined the cost of several drugs in terms of the cost per month per patient who reaches a PASI 75 response. Even when cost-adjusted for recommended lab monitoring,

Table 7.4 Efficacy of DMARDS and biologics for the treatment of psoriasis and PsA

Drug	Molecular Target	Psoriasis dosing	Evidence for efficacy in psoriasis	FDA approved for psoriasis	PsA dosing	Evidence for efficacy in PsA	FDA-approved for PsA
Methotrexate	Dihyrofolate reductase and thymidylate synthetase	10-25 mg PO/IM/SC qwk	Yes	Yes	10-25 mg PO/IM/SC qwk	Yes	No
Acitretin	Retinoic acid receptors	10–50 mg PO daily	Yes	Yes	N/A	No	No
Leflunomide	Dihydroorotate dehydrogenase	N/A	Minimal	No	20 mg daily	Yes	No
Cyclosporine	Cyclophilin	2–5 mg/kg PO daily	Yes	Yes	N/A	No	No
Apremilast	PDE4	30 mg PO BID	Yes	Yes	30 mg PO BID	Yes	Yes
Etanercept	TNF-α	50 mg SC BIW × 12wks, then qwk	Yes	Yes	50 mg SC qwk	Yes	Yes
Adalimumab	TNF-α	80 mg SC ×1 then in 7 days 40 mg SC q2wks	Yes	Yes	40 mg SC q2wks	Yes	Yes
Infliximab	TNF-α	5 mg/kg IV at weeks 0, 2, 6 then q8wks	Yes	Yes	5 mg/kg IV at weeks 0, 2, 6 then q8wks	Yes	Yes
Golimumab	TNF-α	50 mg SC q4wks or 2 mg/kg IV at week 0, 4 and then q8wks	Yes	No	50 mg SC q4wks or 2 mg/kg IV at week 0, 4 and then q8wks	Yes	Yes
Certolizumab	TNF-α	400 mg SC q2wks	Yes	Yes	400 mg SC q2wks × 3 doses then 200 mg q2wks OR 400 mg q4wks	Yes	Yes

Table 7.4 (continued)

Drug	Molecular Target	Psoriasis dosing	Evidence for efficacy in psoriasis	FDA approved for psoriasis	PsA dosing	Evidence for efficacy in PsA	FDA-approved for PsA
Ustekinumab	IL-12/23 p40	45 mg SC at week 0, 4 then q12wks (if >100 kg, use 90 mg)	Yes	Yes	45 mg SC at wk 0, 4 then q12wks (if >100 kg, use 90 mg)	Yes	Yes
Secukinumab	IL-17A	300 mg SC qwk ×5 wks then q4wks	Yes	Yes	150–300 mg SC qwk ×5 wks then q4wks	Yes	Yes
Ixekizumab	IL-17A	160 mg SC at week 0, then 80 mg SC at weeks 2, 4, 6, 8, 10, 12, then q4wks	Yes	Yes	160 mg SC at wk 0, then 80 mg SC q4wks	Yes	Yes
Brodalumab	IL-17 receptor	210 mg SC at wks 0, 1, 2 then q2wks	Yes	Yes	140 mg or 280 mg SC at wks 0, 1, 2, then q2wks	Yes	No
Abatacept	CD80/CD86	N/A	No	No	125 mg SC q1wk OR 500–1000 mg IV q4wks	Yes	Yes
Guselkumab	IL-23 p19	100 mg SC at wk 0 and 4, then q8wks	Yes	Yes	100 mg SC at wk 0 and 4, then q8wks	Yes	Yes
Risankizumab	IL-23 p19	150 mg SC at wk 0 and 4, then q12wks	Yes	Yes	N/A	N/A	No
Tofacitinib	JAK1/JAK3	N/A	No	No	5 mg PO BID OR 11 mg daily	Yes	Yes

MTX was the most cost-effective option at $794.05-1,502.51 per month. The most expensive therapies were infliximab and ustekinumab 90 mg, costing $8,704.68-15,235.52 and $12,505.26-14,256.75 monthly, respectively (Table 7.4) [216].

References

1. Parisi R, Symmons DPM, Griffiths CEM, Ashcroft DM. Global epidemiology of psoriasis: a systematic review of incidence and prevalence. J Invest Dermatol. 2012; https://doi.org/10.1038/jid.2012.339.
2. O'Neill T, Silman AJ. Psoriatic arthritis. Historical background and epidemiology. Baillieres Clin Rheumatol. 1994;8(2):245–61. http://www.ncbi.nlm.nih.gov/pubmed/8076386. Accessed April 15, 2015.
3. Alenius G-M, Stenberg B, Stenlund H, Lundblad M, Dahlqvist SR. Inflammatory joint manifestations are prevalent in psoriasis: prevalence study of joint and axial involvement in psoriatic patients, and evaluation of a psoriatic and arthritic questionnaire. J Rheumatol. 2002;29(12):2577–82. http://www.ncbi.nlm.nih.gov/pubmed/12465155. Accessed April 15, 2015.
4. Harrison BJ, Silman AJ, Barrett EM, Scott DG, Symmons DP. Presence of psoriasis does not influence the presentation or short-term outcome of patients with early inflammatory polyarthritis. J Rheumatol. 1997;24(9):1744–9. http://www.ncbi.

of organ toxicity and require regular laboratory monitoring (Table 25.3). Methotrexate and acitretin are also pregnancy category X; in fact, females should not become pregnant for 3 years following the last dose of acitretin.

Apremilast is a newer oral agent approved for both psoriasis and psoriatic arthritis in 2014. Apremilast binds to and inhibits phosphodiesterase-4, which is responsible for turning on the inflammatory cascade implicated in the pathogenesis of psoriasis. Unlike methotrexate, cyclosporine, and acitretin, apremilast has no known risks of organ toxicity and thus requires no monitoring tests (although dose should be adjusted for decreased renal function).[51]

Biologic Therapy

Biologic agents are immunomodulating monoclonal antibodies that bind to specific targets of the immune system. In the last decade, biologic therapies have revolutionized the treatment of psoriasis, and furthermore, they have shed new insight into the immunopathogenesis of psoriasis and other immune-mediated diseases. There are currently three classes of biologic agents approved by the FDA for the treatment of moderate-to-severe psoriasis. This includes the TNF-α inhibitors etanercept (Enbrel), adalimumab (Humira), and infliximab (Remicade); IL-12/23-inhibitor ustekinumab (Stelara); and IL-17A inhibitors secukinumab (Cosentyx) and ixekizumab (Taltz). All of these medications are administered as subcutaneous injections except for infliximab, which is administered as an infusion. Although infliximab may be one of the most effective biologic agents to date,[52] the inconvenience of infusions and loss of efficacy over time can limit its use. The newer anti-IL 17 agents have also shown great efficacy.[53] The dosing regimens of each of the biologic agents are shown in Table 25.4.

Table 25.4: Biologic agents for the treatment of psoriasis.

Name	*Target*	*Dosing*	*Possible adverse reactions*	*Warnings and precautions*
Etanercept	TNF-alpha	50 mg SQ BIWx3 months, then 50 mg QW	Infections Injection site reactions	Serious infections Malignancy Demyelinating disease Congestive heart failure Cytopenias Hep B reactivation Anaphylaxis Lupus like syndrome Autoimmune hepatitis
Adalimumab	TNF-alpha	80 mg SQ at W0, then 40 mg QOW starting at W1	Infections Injection site reactions Headache Rash	Serious infections Malignancy Anaphylaxis Hep B reactivation Demyelinating disease Cytopenias Congestive heart failure Lupus like syndrome
Infliximab	TNF-alpha	5 mg/kg IV at W0, 2, and 6, then Q8W	Infections Infusion related reactions Headache Abdominal pain	Serious infections Malignancy Hep B reactivation Hepatotoxicity Congestive heart failure Cytopenias Hypersensitivity Cardiovascular and cerebrovascular reactions Demyelinating disease Lupus like syndrome

(Contd...)

(Contd...)

Name	*Target*	*Dosing*	*Possible adverse reactions*	*Warnings and precautions*
Certolizumab Pegol	TNF-alpha	400 mg SQ QOW	Infections Rash	Serious infections Malignancy Congestive heart failure Anaphylaxis Hep B reactivation Demyelinating disease Cytopenias Lupus like syndrome
Ustekinumab	IL12/23	45 or 90 mg SQ at W0, 4, then Q12W	Infections Headache Fatigue	Serious infections Malignancies Hypersensitivity reactions Reverse posterior leukoencephalopathy Noninfectious pneumonia
Guselkumab	IL23	100 mg SQ at W0, 4, then Q8W	Infections Headache Injection site reaction Arthralgia Diarrhea Gastroenteritis Tinea infections Herpes simplex infections	Serious infections
Tildrakizumab	IL23	100 mg SQ at W0, 4, then Q12W	Infections Injection site reactions Diarrhea	Hypersensitivity Serious infections
Secukinumab	IL17A	300 mg SQ at W0, 1, 2, 3, 4, then Q4W	Infections Diarrhea	Serious infections Inflammatory bowel disease Hypersensitivity reactions
Ixekizumab	IL17A	160 mg SQ at W0, then 80 mg at W2, 4, 6, 8, 10, and 12, then 80 mg Q4W	Injection site reactions Infections Nausea Tinea infections	Serious infections Hypersensitivity Inflammatory bowel disease
Brodalumab	IL17RA	210 mg SQ at W0, 1, 2, then Q2W	Arthralgia Headache Fatigue Diarrhea Oropharyngeal pain Nausea Myalgia Injection site reactions Influenza Neutropenia Tinea infections	Suicidal ideation and behavior Serious infections Inflammatory bowel disease

Given its immunomodulatory effects, active or chronic infectious diseases such as tuberculosis, hepatitis B and C, and HIV should be ruled out prior to initiation of biologic agents. Tuberculosis screening is also recommended yearly. Although controversial, some biologic agents may increase risks of serious infection, demyelinating disease, heart disease, and malignancy as seen with TNF-α inhibitors.[54] New-onset psoriasis in patients with no previous history of psoriasis,[55] cutaneous small vessel vasculitis,[56] granulomatous eruptions,[57] eczematous

Table 29.1 Advantages and disadvantages of systemic agents for the treatment of psoriasis in the elderly population

Medications	Advantages	Disadvantages
Acitretin	Lack of immunosuppression or increased malignancy risk, decreased risk of nonmelanoma skin cancer, oral option	Delay in onset by several weeks, mucocutaneous irritation/xerosis, hyperlipidemia, transaminitis (especially in the setting of alcohol intake), contraindicated in severe renal or hepatic dysfunction
Methotrexate	Low cost, oral/intramuscular/subcutaneous options	Dose modification with decreased renal function, nausea, myelosuppression, hepatotoxicity (increased in the setting of alcohol intake), medication interactions (e.g., NSAIDs, antibiotics)
Cyclosporine	Rapid onset, oral option	Immunosuppression, hypertension, renal insufficiency, electrolyte abnormalities, increased risk for skin malignancies, medication interactions (e.g., statins, ACE inhibitors, and potassium-sparing diuretics)
Mycophenolate Mofetil	No dose adjustment in renal disease, oral option	Hematologic toxicity, diarrhea/abdominal pain, dose adjustment in hypoalbuminemia, medication interactions (e.g., phenytoin, salicylates, antiviral medications)
Etanercept	No age-dependent increase in adverse events, minimal medication interactions, good long-term safety data	Worsened CHF, immunosuppression, reactivation of tuberculosis and hepatitis B, possible increase in lymphoproliferative diseases, demyelinating disorders
Infliximab	Minimal medication interactions	Worsened CHF, immunosuppression, reactivation of tuberculosis and hepatitis B, possible increase in lymphoproliferative diseases, demyelinating disorders, infusion reactions, logistics of infusions
Adalimumab	Minimal medication interactions	Worsened CHF, immunosuppression, reactivation of tuberculosis and hepatitis B, possible increase in lymphoproliferative diseases, demyelinating disorders
Ustekinumab	Minimal medication interactions, decreased frequency of injections	Less long-term safety data than TNF-inhibitors, immunosuppression, rate of serious infections directly related to age and diabetes, controversial trend toward increased risk for MACE
Secukinumab	Minimal medication interactions	Limited long-term safety data, immunosuppression, increased risk for candida infections, worsened IBD
Ixekizumab	Minimal medication interactions	Limited long-term safety data, immunosuppression, myelosuppression, increased risk for candida infections, worsened IBD
Apremilast	Lower infection risk, no lab monitoring except if baseline renal status unknown, weight loss, oral option	Limited long-term safety data, dose adjustments for creatinine clearance, possible drug interactions with C450 enzyme inducers (e.g., Rifampin), diarrhea, weight loss, depression/suicidal ideation

Table 32.1 (continued)

Treatment	Population	Dosing	Duration of treatment	Side effects	Overall recommendation
Mycophenolate mofetil	Adult	No official recommendations [22]. *Anecdotally* Twice daily dosing: 0.5–3.0 g/day [44]	Maximum: no official recommendation [22] Minimum: clinical improvement has been noted within 4 weeks of treatment [44]	Common: mild headache, gastrointestinal disturbances, fatigue [44] Rare: hematologic and genitourinary symptoms [22]	*For EC-MPS specifically* Very weak recommendation is possible for EC-MPS as a maintenance treatment for severe AD after induction of remission by CsA for long-term use up to 30 weeks [1]
	Pediatric	*Young children* Twice daily dosing [45]: 40–50 mg/kg/day [6] Adolescents Twice daily dosing [45]: 30–40 mg/kg/day [6]			
Oral corticosteroids	Adult and pediatric	0.75–1 mg/kg per day (prednisone, prednisolone)	Minimum: 3 days Maximum: 3 weeks	Diabetes, hypertension, gastric ulcers, osteoporosis, glaucoma, opportunistic infections and Cushing syndrome Pediatric: decreased growth velocity	Not recommended. May be used in short-term (up to 1 week, maximum 3 weeks) for acute flares in exceptional and severe cases of AD

Table 32.2 Oral agents in development for atopic dermatitis.

New agent	Mechanism of action	Phase of development	Current trials
Apremilast	PDE4 inhibitor	Phase 2, completed	NCT02087943
Fevipiprant (QAW 039)	CRTH2 antagonist	Phase 2, completed	NCT01785602
PF 04965842	JAK 1 inhibitor	Phase 2	NCT02780167
DGLA	Regulation of PGD1	Phase 2	NCT02864498
Tradipitant (VLY-686, LY686017)	NK-1R antagonists	Phase 2	NCT02004041 NCT02651714
ZPL-389 (ZPL-3803787)	H4R antagonist	Phase 2	NCT02424253

CRTH2 chemoattractant receptor-homologous molecule expressed on T-helper type 2 cells, *DGLA* dihomo-gamma-linolenic acid, *H4R* histamine H4 receptor, *JAK* Janus kinase, *PDE4* phosphodiesterase-4, *PGD1* prostaglandin D1, *NK-1R* neurokinin 1 receptor

Case Report

A 42-year-old white male presents with a lifelong history of "eczema," which has flared over the past few years. He was previously managed with topical agents but these have not been working for him lately. He complains of severe itching, which interrupts his sleep. Given the night shift at work, he finds it difficult to sleep during the day with ongoing itch and has been having difficulty coping. He notes he has been "short" and "moody" with his family and attributes this to lack of sleep. There is a family history of atopic dermatitis in his daughter as well.

Past Medical History

- Hypertension
- Anxiety
- Asthma

Social History

- Drinks socially
- Married, 2 children
- Floor manager at a distribution plant, working shift work, mainly night shifts

Previous Therapies

- Topical steroids

Physical Exam

- Erythematous excoriated lichenified plaques on the wrists, antecubital and popliteal fossae; facial erythema and scaling with Dennie-Morgan folds noted

Management

Due to the severity of his atopic dermatitis flare and his difficulty coping, systemic therapy with cyclosporine was initiated at 150 mg PO BID. He is also managed with topical tacrolimus 0.1% ointment BID for the face/body and betamethasone valerate 0.1% ointment for the body flares prn. He has good control of his skin with improved sleep while taking cyclosporine but because of his hypertension, his dose is reduced to 100 mg PO BID when possible. To manage flares in symptoms he intermittently increases back to 150 mg PO BID with close monitoring.

References

1. Roekevisch E, Spuls PI, Kuester D, Limpens J, Schmitt J. Efficacy and safety of systemic treatments for moderate-to-severe atopic dermatitis: a systematic review. J Allergy Clin Immunol. 2014;133(2):429–38. https://doi.org/10.1016/j.jaci.2013.07.049.
2. Schmitt J, Schmitt NM, Kirch W, Meurer M. Outpatient care and medical treatment of children and adults with atopic

Downloaded from http://journals.lww.com/idoj by BhDMf5ePHKav1zEoum1tQfN4a+kJLhEZgbsIHo4XMi0hCywCX1AWnYQp/IlQrHD3i3D0OdRyi7TvSFl4Cf3VC4/OAVpDDa8KKGKV0Ymy+78= on 12/28/2024

Supplementary Table 1: Biologics and small molecules for nail psoriasis (NP) and alopecia areata nail dystrophy (NAA)*,†

Name	Drug Class	Mechanism of Action	US FDA Approval for Dermatologic Indications	Evidence for Inflammatory Nail Disease	Highest LoE for Inflammatory Nail Disorder Treatment	US FDA Administration/ Dosage/Frequency	US FDA Most Common Adverse Reactions	US FDA Warnings and Precautions
Apremilast	Small Molecule	Phosphodiesterase-4 Inhibitor	Plaque psoriasis, psoriatic arthritis (PsA)[6]	NP	Level 1 – systematic review and crossover	Oral/18+/30 mg BID after day 6; renal dosing advised	(<5%) Diarrhea, nausea, headache, upper respiratory tract infection (URTI)[7]	Hypersensitivity, depression, weight decrease, drug interactions, severe diarrhea, nausea, vomiting
Deucravacitinib	Small Molecule	Allosterically inhibits tyrosine kinase 2 in the JAK-STAT pathway[8]	Plaque psoriasis[9]	NP	Level 5 – no significance in meta-analysis	Oral/18+/6 mg daily	(≥1%) URTI, elevated blood creatinine phosphokinase (CPK), herpes simplex, mouth ulcers, folliculitis, acne	Hypersensitivity, infections, tuberculosis, malignancy, rhabdomyolysis and elevated CPK, laboratory abnormalities, immunization interactions, higher rates of all-cause mortality related to JAK inhibition
Tofacitinib	Small Molecule	Targets JAK1, JAK2, and JAK3 enzymes, inhibiting the JAK-STAT signaling pathway[10]	PsA[11]	NP, NAA	NP: Level 1 – systematic review NAA: Level 4 – case control study	Oral/18+/Tofacitinib 5 mg BID or Tofacitinib extended release XR 11 mg once daily; renal and hepatic dosing advised	(≥5%) URTI, nasopharyngitis, diarrhea, headache	Serious infections, tuberculosis, malignancy, gastrointestinal perforations, laboratory abnormalities and immunization interactions Black box warning for heart-related events, cancer, thrombosis, and death Contraindicated in breastfeeding; Combination with potent immunosuppressants not recommended
Upadacitinib	Small Molecule	Selective JAK1 inhibitor	PsA, atopic dermatitis[12]	NP	Level 3 – observational study without dramatic effect	Oral/12+/15mg once daily; pediatric, renal and co-usage of CYP3A4 inhibitor dosing may be advised	PsA(≥1%):URTI, herpes zoster, herpes simplex, bronchitis, nausea, cough, pyrexia, acne and headache Atopic Dermatitis (≥1%): URTI, acne, herpes simplex, headache, increased, CPK, cough, hypersensitivity, folliculitis, nausea, abdominal pain, pyrexia, increased weight, herpes zoster, influenza, fatigue, neutropenia, myalgia, and influenza-like illness[13]	Hypersensitivity, gastro intestinal perforations, laboratory abnormalities, embryo-fetal toxicity Black box warning for serious infections, mortality, malignancy, cardiovascular death, and thrombosis[14] Contraindicated in severe hepatic impairment; use with immunosuppressants or JAK inhibitors, live vaccines, and strong cytochrome P450 3A4 (CYP3A4) inhibitors not recommended

Contd...

Downloaded from http://journals.lww.com/idoj by BhDMf5ePHKav1zEoum1tQfN4a+kJLhEZgbsIHo4XMi0hCywCX1AWnYQp/IlQrHD3i3D0OdRyi7TvSFl4Cf3VC4/OAVpDDa8KKGKV0Ymy+78= on 12/28/2024

Supplementary Table 1: Contd...

Name	Drug Class	Mechanism of Action	US FDA Approval for Dermatologic Indications	Evidence for Inflammatory Nail Disease	Highest LoE for Inflammatory Nail Disorder Treatment	US FDA Administration/ Dosage/Frequency	US FDA Most Common Adverse Reactions	US FDA Warnings and Precautions
Adalimumab	Biologic	TNF-inhibitor (recombinant human IgG1 (Immunoglobulin G) monoclonal antibody)[15]	Plaque psoriasis, PsA, NP, Hidradenitis Suppurativa[16]	NP	Level 1 – systematic review	2+/Subcutaneous/ PsA: 40 mg every other week Plaque Psoriasis: 40 mg every other week starting one week after initial dose	(>10%): infections, injection site reactions, headache, rash	Serious infections, tuberculosis, malignancy, invasive fungal infection, hypersensitivity reaction, Hepatitis B reactivation, demyelinating disease, cytopenia, heart failure, and lupus-like syndrome
Certolizumab Pegol	Biologic	TNF-inhibitor (humanized Fab' antibody fragment that binds to and blocks TNF-alpha)	Plaque psoriasis, PsA[17]	NP	Level 1 – systematic review	18+/Subcutaneous/ Plaque Psoriasis: 400 mg (given as 2 subcutaneous injections of 200 mg each) every other week. Dosing for body weight advised. PsA: 200 or 400 mg every other week after week 4	(>7%): URTI, rash, urinary tract infection	Serious infections, tuberculosis, invasive fungal infections, malignancy, heat failure, hypersensitivity reaction, Hepatitis B reactivation, demyelinating disease, cytopenias, lupus-like syndrome
Etanercept	Biologic	TNF-inhibitor (human dimeric fusion protein that competitively binds to and inhibits TNF-alpha and TNF-beta[18])	Plaque psoriasis, PsA[19]	NP	Level 1 – systematic review	2+/Subcutaneous/ Plaque Psoriasis: 50 mg once weekly after 3 months Pediatric dosing advised. PsA: 50 mg once weekly with or without methotrexate (MTX)	(>5%): infections and injection site reactions	Serious infection, tuberculosis, malignancy, invasive fungal infection, demyelinating disease, congestive heart failure, pancytopenia or aplastic anemia, Hepatitis B reactivation, hypersensitivity reaction, lupus-like syndrome Use with live vaccines, anakinra, abatacept, and cyclophosphamide not recommended[20]
Golimumab	Biologic	TNF-Inhibitor (human IgG1 monoclonal antibody that blocks TNF-alpha)[21]	PsA[22]	NP	Level 1 – crossover and systematic review	18+/Subcutaneous or IV infusion/ Subcutaneous 50 mg once per month; IV infusion 2 mg/kg at weeks 0 and 4, and every 8 weeks thereafter	(>5%): URTI, nasopharyngitis[23]	Serious infections, invasive fungal infections, Hepatitis B reactivation, malignancy, heart failure, demyelinating disease, hypersensitivity reactions

Contd...

Downloaded from http://journals.lww.com/idoj by BhDMf5ePHKav1zEoum1tQfN4a+kJLhEZgbsIHo4XMi0hCywCX1AWnYQp/IlQrHD3i3D0OdRyi7TvSFl4Cf3VC4/OAVpDDa8KKGKV0Ymy+78= on 12/28/2024

Supplementary Table 1: Contd...

Name	Drug Class	Mechanism of Action	US FDA Approval for Dermatologic Indications	Evidence for Inflammatory Nail Disease	Highest LoE for Inflammatory Nail Disorder Treatment	US FDA Administration/ Dosage/Frequency	US FDA Most Common Adverse Reactions	US FDA Warnings and Precautions
Infliximab	Biologic	TNF-inhibitor (recombinant humanized monoclonal TNF-alpha antibody[24])	Plaque psoriasis, PsA	NP	Level 1 – systematic review	6+/Intravenous/5 mg/kg every 8 weeks after week 6	(>10%): infections (ex. URTI, sinusitis, pharyngitis), infusion-related reactions, headache, abdominal pain[25]	Serious infections, invasive tuberculosis, fungal infections, malignancy, Hepatis B reactivation, hepatotoxicity, heart failure, cytopenias, hypersensitivity, cardiovascular and cerebrovascular reactions, demyelinating disease, lupus-like syndrome Use with live vaccines not recommended Doses >5 mg/kg contraindicated in patients with moderate-to-severe heart failure
Bimekizumab	Biologic	IL-17 Inhibitor (binds the IL-17A, IL-17F, and the IL-17A & F heterodimer[26]	Plaque psoriasis[27]	NP	Level 2- randomized control	18+/ Subcutaneous/320 mg (two 160 mg injections) every 8 weeks after week 16. Weight based dosing advised.	(≥1%): URTI, oral candidiasis, headache, injection site reactions, tinea, gastroenteritis, herpes simplex, acne, folliculitis, other candida infections, fatigue	Suicidal ideation and behavior, serious infections, tuberculosis, liver enzyme abnormalities, IBD
Brodalumab	Biologic	IL-17 Inhibitor (fully human monoclonal IgG2 antibody[28])	Plaque psoriasis[29]	NP	Level 1- systematic review	18+/ Subcutaneous/210 mg every 2 weeks after week 2	(≥1%): arthralgia, headache, fatigue, diarrhea, oropharyngeal pain, nausea, myalgia, injection site reactions, influenza, neutropenia, tinea	Serious infections, tuberculosis, Crohn's disease Black box warning for suicidal ideation and behavior. Contraindicated in Crohn's Disease Use with live vaccines not recommended
Ixekizumab	Biologic	IL-17 Inhibitor (humanized IgG4 monoclonal antibody[30])	Plaque psoriasis, PsA[31]	NP	Level 1 – systematic review	6+/Subcutaneous/ Plaque Psoriasis: 80 mg every 4 weeks after week 12 PsA: 80 mg every 4 weeks after initial dose	(≥1%): injection site reactions, URTI, nausea, tinea	Serious infections, tuberculosis, IBD Use with live vaccines not recommended

Contd...

Downloaded from http://journals.lww.com/idoj by BhDMf5ePHKav1zEoum1tQfN4a+kJLhEZgbsIHo4XMi0hCywCX1AWnYQp/IlQrHD3i3D0OdRyi7TvSFl4Cf3VC4/OAVpDDa8KKGKV0Ymy+78= on 12/28/2024

Supplementary Table 1: Contd...

Name	Drug Class	Mechanism of Action	US FDA Approval for Dermatologic Indications	Evidence for Inflammatory Nail Disease	Highest LoE for Inflammatory Nail Disorder Treatment	US FDA Administration/ Dosage/Frequency	US FDA Most Common Adverse Reactions	US FDA Warnings and Precautions
						Pediatric and concomitant Plaque Psoriasis and PsA dosing advised.		
Secukinumab	Biologic	IL-17 inhibitor (human IgG1[32])	Plaque psoriasis, PsA[33]	NP	Level 1- systematic review	6+/ Subcutaneous (plaque psoriasis), Subcutaneous or Intravenous (PsA)/ Plaque psoriasis: 150 or 300 mg every 4 weeks after week 4. PsA: Subcutaneous: With a loading dose: 150 mg every 4 weeks after week 4 Without loading dose: 150 mg every 4 weeks Dosage of 300 mg every 4 weeks can be considered for continued active PsA Intravenous: With a loading dosage: 1.75 mg/kg every 4 weeks after loading dose Without a loading dosage: 1.75 mg/kg every 4 weeks Dosing for pediatric and concomitant plaque psoriasis and PsA advised.	(>1%): nasopharyngitis, diarrhea, URTI	Serious infections, tuberculosis, IBD, hypersensitivity reactions Use with live vaccines not recommended

Contd...

Downloaded from http://journals.lww.com/idoj by BhDMf5ePHKav1zEoum1tQfN4a+kJLhEZgbsIHo4XMi0hCywCX1AWnYQp/IlQrHD3i3D0OdRyi7TvSFl4Cf3VC4/OAVpDDa8KKGKV0Ymy+78= on 12/28/2024

Supplementary Table 1: Contd...

Name	Drug Class	Mechanism of Action	US FDA Approval for Dermatologic Indications	Evidence for Inflammatory Nail Disease	Highest LoE for Inflammatory Nail Disorder Treatment	US FDA Administration/ Dosage/Frequency	US FDA Most Common Adverse Reactions	US FDA Warnings and Precautions
Guselkumab	Biologic	IL-23 Inhibitor (human immunoglobulin G1 lambda (IgG1λ) monoclonal antibody[34])	Plaque psoriasis	NP	Level 1 – systematic review and crossover	18+/ Subcutaneous/100 mg every 8 weeks after week 4	(>1%): nasopharyngitis, diarrhea, URTI[35]	Serious infections, tuberculosis, IBD, hypersensitivity reactions Use with live vaccines not recommended
Risankizumab	Biologic	IL-23 Inhibitor (humanized IgG monoclonal antibody that selectively inhibits the p19 subunit[36])	Plaque psoriasis, PsA[37]	NP	Level 1- systematic review	18+/ Subcutaneous/150 mg every 12 weeks after week 4	(≥1%): URTI, headache, fatigue, injection site reactions, tinea[38]	Hypersensitivity reactions, serious infections, tuberculosis Use with live vaccines not recommended
Tildrakizumab	Biologic	IL-23 Inhibitor (humanized monoclonal IgG1κ antibody that selectively binds the p19 subunit[39])	Plaque psoriasis	NP	Level 1 - systematic review	18+/ Subcutaneous/100 mg every twelve weeks after week 4	(≥1%): URTI, injection site reactions, diarrhea	Hypersensitivity, serious infections, tuberculosis
Ustekinumab	Biologic	IL-23 Inhibitor (human monoclonal antibody that binds to IL-12Rβ1, which inhibits IL-12 and IL-23[40])	Plaque psoriasis and PsA[41]	NP	Level 1 – systematic review and crossover	6+/Subcutaneous/45 mg every 12 weeks after week 4 Pediatric and concomitant plaque psoriasis dosing advised.	(>3%): nasopharyngitis, URTI, headache, fatigue[42]	Serious infections, tuberculosis, malignancy, hypersensitivity reactions, Reversible Posterior Leukoencephalopathy Syndrome

*Note that hypersensitivity reactions can occur with all biologic and small-molecule drugs for inflammatory nail disease. †This table contains limited information. Details about dosing, including loading dosages, indications, and side effects should be obtained from trained physicians and US FDA-approved sources

My publications

Dermatology diseases Index

FIRST INDEX OF SKIN DISEASES IN THE WORLD

Dr. Hany Salah Soliman
Mansoura Dermatology
& Leprosy Hospital, Egypt

COPYRIGHTED

Dermatology Diseases Atlas

With hyperlinks to images folders
E12 2025-29 october
educational ,Non-profit aim only

H.S.S-Mansoura-Egypt`

1- Dermoscopy (153)
2- Nail (144)
3- Pathology (291)
4- Diseases of skin and mucous membrane (1719)

Whatsapp +201061732403

Tables in Dermatology

+15 THOUSANDS TABLES

H.S.S-Mansoura-Egypt`

Whatsapp +201061732403

Index of treasures

1-	Phenomena in dermatology
2-	Locus minoris resistentiae
3-	Collision of tumours
4-	Unusual location of common dermatosis
5-	Unusual color of common dermatosis
6-	Unusual pattern (heart shaped..etc)
7-	Common mimickers
8-	Post herpes zoster phenomena and dermatosis
9-	Co-localization of more than one dermatosis
10-	Co-existence of more than one dermatosis
11-	Collections in dermatology
12-	Criteria in dermatology
13-	18 thousand tables in dermatology
14-	Zosteriform lesions